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Preliminary Evaluations of Initial TSCA (Toxic Substances Control Act) Section 8 (e) Substantial Risk Notices January 1, 1983 to December 31, 1984

(U.S.) Environmental Protection Agency
Washington, DC

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Agency

Office of Pesticides
and Toxic Substances
Washington DC 20460

March 1985
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Toxic Substances

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Preliminary Evaluations of Initial TSCA Section 8(e) Substantial Risk Notices

2, February 1, 1983 - December 31, 1984

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This volume contains, in ascending submission number order, "status report" (i.e., preliminary evaluations) prepared by staff of the Office of Toxic Substances in EPA's Office of Pesticides and Toxic Substances for initial submissions received by EPA from chemical manufacturers, importers, processors, and distributors from January 1, 1983 to December 31, 1984 under Section 8(e), the "substantial risk" information reporting provision of the Toxic Substances Control Act (TSCA). The status reports contained in this compendium reflect only the initial phases of EPA's evaluation process for the submitted information.

This TSCA Section 8(e) status report volume has been published by the Agency for two reasons. First, a volume of Section 8(e) status reports with appropriate indices will make the submitted information more accessible. Second, this volume may, by providing specific examples of submitted information and EPA's preliminary evaluation of that information, help those persons subject to Section 8(e) understand better the types of information that should be submitted to EPA pursuant to this mandatory reporting provision of TSCA.

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March 1985

PRELIMINARY EVALUATIONS OF INITIAL TSCA SECTION 8(e) SUBSTANTIAL RISK NOTICES

JANUARY 1, 1983 TO DECEMBER 31, 1984

Office of Toxic Substances
Office of Pesticides and Toxic Substances
Washington, D.C. 20460

U.S. ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PESTICIDES AND TOXIC SUBSTANCES
WASHINGTON, D.C. 20460

Disclaimer

This volume has been reviewed by the Office of Pesticides and Toxic Substances (OPTS), U.S. Environmental Protection Agency, and approved for publication. The status reports contained in this volume present the Agency's preliminary evaluations of the submitted information and do not represent final Agency policy or intent with respect to the submissions or subject chemicals. Mention of company names, trade names, or commercial products does not constitute an Agency endorsement or recommendation for or against use.

Foreward

This volume contains, in ascending submission number order, "status reports" (i.e., preliminary evaluations) prepared by staff of the Office of Toxic Substances (OTS) in the Office of Pesticides and Toxic Substances (OPTS) for initial submissions received by EPA from chemical manufacturers, processors, and distributors between January 1, 1983, and December 31, 1984, pursuant to Section 8(e), the "substantial risk" information reporting provision of the Toxic Substances Control Act (TSCA; 90 Stat. 2029, 15 U.S.C. 2607(e)). Status reports are prepared by OTS for all initial TSCA Section 8(e) submissions and reflect only part of the initial phase of the OTS evaluation process for such information.

This volume is being distributed through the TSCA Assistance Office (TAO) in OTS/OPTS. Persons wishing to obtain a copy of this volume of Section 8(e) status reports should telephone TAO (toll-free: 800-424-9065 or, in Washington, D.C.: 554-1404), or write to:

TSCA Assistance Office (TS-799)
U.S. Environmental Protection Agency
401 "M" Street, S.W.
Washington, D.C. 20460

The Agency plans to print a limited number of copies of this volume. After the Agency's supply is exhausted, copies can be purchased through the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, Virginia 22161. Copies of the three previously published Section 8(e) status report volumes (PB# 80-221609, PB# 81-145732 and PB #83-187815) are currently available through NTIS.

The Agency welcomes the submission of additional information for, or comments on, the evaluations presented in this volume. The submission of unpublished information relating to biological or environmental effects, production/importation volumes, use(s), and worker, consumer, and environmental exposure to the subject chemical substances and mixtures would be especially valuable. Such information will be considered at subsequent steps in the OTS chemical assessment process. The submission of additional information for, or comments on, these evaluations should be directed to:

Mr. Frank D. Kover, Chief
Chemical Screening Branch
Existing Chemical Assessment Division (TS-778)
Office of Toxic Substances/OPTS
U.S. Environmental Protection Agency
401 "M" Street, S.W.
Washington, D.C. 20460

All TSCA Section 8(e) submissions as well as EPA status reports can be viewed in the OPTS public files (subject to claims of confidentiality made by submitting companies). The OPTS public files are located at EPA Headquarters (Room 107, East Tower), 401 "M" Street, S.W., Washington, D.C. Persons wishing to obtain copies of actual TSCA Section 8(e) submissions should write to EPA's Freedom of Information Office at the following address and include the desired Section 8(e) submission numbers.

Freedom of Information Office (A-101)
U.S. Environmental Protection Agency
401 "M" Street, S.W.
Washington, D.C. 20460

This and previous volumes of Section 8(e) status reports have been published by EPA for two reasons. First, volumes of 8(e) status reports will make reported information more accessible. Second, such volumes may, by providing specific examples of submitted information and EPA's evaluation of that information help those persons subject to Section 8(e) to understand better the types of information that should be submitted.

J Merenda

Joseph J. Merenda, Director
Existing Chemical Assessment Division
Office of Toxic Substances/OPTS/EPA

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Acknowledgment

In preparing the status reports contained in this compendium, EPA's Office of Toxic Substances (OTS) has frequently found it necessary to request additional information about, or clarification of, the submitted data. OTS appreciates the efforts and cooperation of the following companies and organizations that have submitted the information reflected in this volume:

3M COMPANY
AIR PRODUCTS AND CHEMICALS, INC.
ALLIED CORPORATION
AMERICAN CYANAMID COMPANY
ANGUS CHEMICAL COMPANY
CELANESE CORPORATION
CHEVRON CHEMICAL COMPANY
CHLORINATED PARAFFIN PRODUCERS TESTING CONSORTIUM
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Introduction

Section 8(e) of the Toxic Substances Control Act (TSCA; the Act) states that "any person who manufactures, processes, or distributes in commerce a chemical substance or mixture and who obtains information which reasonably supports the conclusion that such substance or mixture presents a substantial risk of injury to health or the environment shall immediately inform the [EPA] Administrator of such information unless such person has actual knowledge that the Administrator has been adequately informed of such information."

In view of the fact that Section 8(e) was self-implementing (i.e., required no implementing rules), chemical manufacturers, processors, and distributors became subject to the Section 8(e) reporting provision as of January 1, 1977, the effective date of TSCA. In order to clarify the types of information to be submitted and the procedures for doing so, EPA (following receipt and review of public comments) published its March 16, 1978 TSCA Section 8(e) policy statement ("Statement of Interpretation and Enforcement Policy; Notification of Substantial Risk" 43 FR 11110). For easy referral when using this volume, EPA's TSCA Section 8(e) policy statement has been reproduced as Appendix A in the back of this volume.

The March 16, 1978 TSCA Section 8(e) policy statement expresses the Agency's policy that the information subject to Section 8(e) reporting is any "new" information that "reasonably supports" a conclusion that a chemical substance or mixture presents a substantial risk of injury to health or the environment but need not necessarily conclusively indicate such risk. A determination of "substantial risk" does not include an evaluation of economic or social benefits of the use of the chemical and, therefore, is not synonymous with the term "unreasonable risk" which is found in other sections of the Act. Although EPA's receipt of information under Section 8(e) of TSCA does not necessarily trigger immediate regulatory action, the information which is submitted under TSCA Section 8(e) does receive priority review and evaluation by EPA in order to determine an appropriate course of Agency action.

Thus far, EPA and the chemical industry have devoted significant efforts in fulfilling their respective responsibilities under Section 8(e) of TSCA. Since January 1, 1977, over 540 initial TSCA Section 8(e) notices covering a broad range of toxicity and exposure-related information on a wide variety of chemicals have been received and given priority evaluation and follow-up attention by the Office of Toxic Substances (OTS) in EPA's Office of Pesticides and Toxic Substances (OPTS). In general, each initial TSCA Section 8(e) submission is promptly reviewed and evaluated by OTS scientific staff in order to determine both the degree of concern that should be attached to the submitted information and the initial course of any warranted OTS follow-up action(s). A "status report" is prepared which contains a brief description of the submitted information, the results of the OTS preliminary evaluation, a statement with respect to the production and use of the subject chemical(s), and the recommendations for appropriate follow-up actions. Upon approval of the status report, recommended follow-up actions are initiated. A letter containing the status report and any Agency requests for additional information is sent to the submitting company. In addition, copies of all status reports are transmitted to the OPTS public files, other designated EPA Program Offices and Federal Agencies, and to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution. Other OTS follow-up actions include the consideration of further, more in-depth assessment of the reported chemical hazard or risk. It should be noted also that the OTS immediately reviews, evaluates, and initiates appropriate follow-up actions/activities for all information contained in "follow-up" and "supplemental" TSCA Section 8(e) notices. By definition, follow-up submissions are those that contain information submitted directly in response to an EPA request, whereas supplemental submissions are those that contain information not specifically requested by EPA.

A Document Control Number is used by EPA to identify TSCA Section 8(e) submissions and takes the following form: 8EHQ-0000-0000. Starting at the left, the first four symbols identify the information as a Section 8(e) submission received by EPA headquarters; the next four digits identify the month and year (e.g., -0579-) of the Agency's receipt of the information; the final four digits identify the submission's chronological number. In addition to the basic numerical sequence, additional characters may be added to the right end of the Document Control Number to convey other information. These additional characters and their meaning are as follows:

S: indicates that the TSCA Section 8(e) submission was sanitized to delete information that was claimed by the submitting company to be "TSCA Confidential Business Information."

P: indicates that the Section 8(e) submission contained names or other identification (e.g., Social Security Numbers) of individuals, the release of which may violate the Privacy Act (such documents are sanitized to remove an individual's name or other identifiers).

*: indicates that, based on a preliminary evaluation, the submission was considered by EPA to be unwarranted for reporting under Section 8(e) of TSCA.

When reviewing the status reports contained in this volume, the reader should realize that the purpose of the OTS preliminary evaluation is to determine the significance of the submitted information in terms of a need for possible follow-up action by the Agency. This determination involves a critical analysis of the submitted data to assess the extent that the reported hazard or risk is supported by the provided information. The scope of this initial evaluation, however, is generally limited to the submitted documents and to any closely related information known by the OTS reviewer. Neither a literature search to identify other reported effects nor an in-depth analysis of possible sources of exposure to subject chemicals is part of the evaluation process. Therefore, a status report should be viewed only as a preliminary evaluation of the submitted information and not as a comprehensive assessment of the chemical substance or mixture for which a TSCA Section 8(e) notice has been filed.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0183-0468
Page 1 of 3

DATE: FEB 28 1983

SUBJECT: Status Report* 8EHQ-0183-0468

Approved 3/1/83

Revision Needed ______

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Submission Description

The Phillips Petroleum Company provided summarized final results from several acute in vivo toxicity studies and final reports from two in vitro mutagenicity assays of carbon black feedstock (Residual Oil Solvent Extracts (Petroleum); CAS No. 64742-10-5). According to the company, the carbon black feedstock displayed mutagenic activity with exogenous metabolic activation in both an Ames/Salmonella typhimurium (bacteria) Assay and a Mouse Lymphoma Forward Mutation Assay; without activation the carbon black feedstock was reported to be negative in both assays. With regard to the results of the acute in vivo carbon black feedstock toxicity studies, Phillips reported that the oral (rat) LD50 was in excess of 5 g/kg and the inhalation (rat) LC50 was in excess of 49.3 parts per million. In addition, Phillips reported that short-term inhalation (mice, head only) exposure to 46.3 ppm vaporized carbon black feedstock did not result in upper respiratory tract irritation. Phillips also reported that no erythema, edema, or other dermal effects were observed at either 24 or 72 hours following carbon black feedstock application to the clipped abraided or unabraided skin of rabbits. (See note on pg. 3 of this status report)

Submission Evaluation

A review of the submitted in vitro data shows that the subject carbon black feedstock, when tested in the presence of exogenous metabolic activation, induced increased mutation frequencies in Salmonella typhimurium bacterial strains TA 98 and TA 1538. In the absence of metabolic activation, although the carbon black feedstock (at the highest dose tested) induced increased mutation frequencies (i.e., 3X and 2.7X background for strains TA 98 and TA 1538, respectively), the observed activity was considerably less than that seen in the bacterial assay conducted in the presence of metabolic activation. Although only summary final data were submitted for the in vitro mouse lymphoma cell assay, it is apparent that the feedstock was mutagenic only in the

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***NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.**

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presence of metabolic activation. Overall, the submitted in vitro mutagenicity results are not necessarily surprising in light of the likely presence of various polynuclear aromatic hydrocarbons (PAH) in the tested carbon black feedstock.

It can be inferred from the summarized acute in vivo toxicity information that the tested carbon black feedstock does not possess serious acute oral toxicity in that no animals died in the 14 days following oral administration. With regard to the results of the acute inhalation test in rats, however, it is not clear if the carbon black feedstock vapor concentration of 49.3 ppm was 1) the maximum attainable concentration and 2) a measured or nominal (i.e., estimated) vapor concentration. Although the summary results of the mouse head-only inhalation exposure study indicate that the tested carbon black feedstock is not an acute upper respiratory tract irritant, there was no rationale given for the dose selected (46.3 ppm) and no indication of whether this concentration was monitored or nominal. In addition, there was no information presented that pertained to the appearance of the eyes or the incidence or duration of eye closure in the mice in the acute head-only inhalation exposure test. With regard to the reported acute rabbit dermal irritation results, although it appears that the carbon black feedstock is not a primary skin irritant, it should be noted that long-term or repeated dermal exposure to the feedstock could result in dissolution and removal of oils that are normally present in the skin. Chronic dermal (or other) exposure to petroleum products containing PAH (some of which are known to possess mutagenic and/or oncogenic activity) would also be of concern. Finally, the inhalation of mists or aspiration of liquid hydrocarbons that might accompany their ingestion and/or regurgitation could result in a chemical pneumonitis. Considering this and the reported lack of toxicity by gavage, the company's Material Safety Data Sheet (MSDS) recommendation that vomiting not be induced following accidental ingestion appears prudent.

Current Production and Use

The tested carbon black feedstock (Residual Oil Solvent Extracts (Petroleum); CAS No. 64742-10-5) is defined by the TSCA Chemical Substances Inventory as "a complex combination of hydrocarbons obtained as the extract from a solvent extraction process. It consists of aromatic hydrocarbons having carbon numbers predominantly higher than C25."

A review of the production range (includes importation volumes) statistics for carbon black feedstock (CAS No. 64742-10-5), which is listed in the initial TSCA Inventory, has shown that over 2.65 billion pounds were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed as confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information that would compromise Confidential Business Information (CBI). The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

Phillips reported that the company does not market carbon black feedstock but either burns the material to produce carbon black or recycles the material back into petroleum refinery streams for further processing. In addition, the company reported that the potential for human exposure to carbon black feedstock is minimal because the feedstock is produced, transported, and consumed in enclosed systems.

Comments/Recommendations

In its submission, the Phillips Petroleum Company stated that based on the submitted test data and the company's knowledge that the carbon black feedstock contains polynuclear aromatic hydrocarbons (PAH), Phillips has classified the feedstock as an indirect-acting mutagen. In addition, Phillips stated that although there is no history of adverse health effects among its employees, the company had revised (and submitted) its carbon black feedstock Material Safety Data Sheet (MSDS) to reflect the submitted information and believes that adherence to the recommended precautions will prevent adverse health effects among those people working with the material. Phillips also reported that the results of a planned in vitro Sister Chromatid Exchange (SCE) assay of carbon black feedstock will be submitted to EPA upon receipt of those results by the company.

EPA has received and evaluated many TSCA Section 8(e) and "For Your Information (FYI)" submissions containing toxicologic and/or exposure information on many petroleum refinery process streams, carbon black, and certain chemical substances (including PAH) associated with petroleum refinery streams and carbon black and/or its production. In addition, the Chemical Hazard Identification Branch has prepared a Chemical Hazard Information Profile (CHIP) on carbon black.

a) The submitted information on carbon black feedstock will be screened by the Chemical Hazard Identification Branch (CHIB/AD/EPA) in order to determine the need for further OTS assessment.

b) The Chemical Hazard Identification Branch will transmit copies of this status report to NIOSH, OSHA, CPSC, FDA, OW/EPA, OSWER/EPA, OANR/EPA and ORD/EPA. Copies of this status report will also be sent to the Industry Assistance Office (IAO/OTS/EPA) and the Office of Toxics Integration OTI/OPTS/EPA) for appropriate distribution.

NOTE: On April 7, 1983 (8EHQ-0483-0468 Supplement), Phillips notified EPA that the tested carbon feedstock was a mixture of light, intermediate, and heavy catalytic cracked petroleum distillates (CAS No.'s: 64741-59-9, 64741-60-2, and 64741-61-3, respectively) and not residual oil solvent petroleum extracts (CAS No. 64742-10-5) as reported in the initial submission.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0283-0469 S
Page 1 of 2

DATE: FEB 28 1983

SUBJECT: Status Report* 8EHQ-0283-0469 S

Approved JK- 3/1/83

Revision Needed ________

FROM: Justine L. Welch, JLW Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Submission Description

(NOTE: The submitting company has claimed its identity and the identities of the subject chemical products to be Confidential Business Information (TSCA CBI)).

The submitting company provided summary results from a lifetime mouse skin-painting study (conducted by the National Institute for Occupational Safety and Health (NIOSH)) involving eleven (11) undiluted metalworking fluid products. The submitting company reported that two of the tested metalworking fluid products were found to be oncogenic to the mouse liver in that higher than chance scores were obtained when the liver data was subjected to two different types of statistical analyses (Chi Square and Fisher Exact Tests). The submitter identified one of the two products as a nitrite/amine synthetic fluid containing a high level of nitrosodiethanolamine (NDELA; CAS No. 1116-54-7); the other product was identified as a non-nitrite synthetic fluid containing no detectable nitrosamines. In addition, the company reported that "none of the other nitrite/amine products in the test gave positive results."

With regard to the observed oncogenic activity, the submitting company stated that:

> "It is important to emphasize that these products were tested in the concentrated form. In normal practice, they would be diluted with water before use and human exposure would be limited to the diluted form only. The nitrite/amine product is recommended for use at a dilution of 1 part of concentrate to 180 parts of water. The non-nitrite product is normally diluted with 20 to 50 parts of water, depending on the application. Since the effect of exposure to the concentrated products was only suggestive, it would be expected that exposure to the diluted product would not involve a significant risk."

***NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.**

Submission Evaluation

In addition to the observed oncogenic activity of a nitrite/amine synthetic metalworking fluid containing a high level of NDELA (a demonstrated animal carcinogen), it is of interest that a non-nitrite synthetic metalworking fluid containing no detectable level of nitrosamines also displayed oncogenic activity. EPA should obtain a copy of the actual study report directly from NIOSH in order to more properly evaluate the reported findings.

Current Production and Use

Metalworking fluids (also known as cutting/grinding fluids) are applied to cutting tools to aid in machine operation by serving as lubricants and/or coolants and by washing away metal chips.

Comments/Recommendations

EPA has received and evaluated several TSCA Section 8(e) and "For Your Information (FYI)" submissions concerning cutting fluids and/or various nitrosamines. In addition, the Chemical Hazard Identification Branch (CHIB/AD/OTS) has prepared Chemical Hazard Information Profiles (CHIPs) on cutting fluids and certain N-nitroso compounds, including nitrosodiethanolamine (NDELA). The OTS "Existing Chemicals Task Force (ECTF)" is currently reviewing toxicity and exposure information on cutting fluids.

a) The Chemical Hazard Identification Branch has requested the National Insitute for Occupational Safety and Health to provide EPA with a complete copy of the final report, including test protocol(s) and data, from the subject lifetime skin-painting study of eleven (11) metalworking fluid products.

b) The Chemical Hazard Identification Branch will transmit copies of this status report to NIOSH, OSHA, CPSC, FDA, OW/EPA, OSWER/EPA, ORD/EPA, OANR/EPA, and to the OTS "Existing Chemicals Task Force (ECTF)." Copies of this report will also be provided to the Office of Toxics Integration (OTI/OPTS/EPA) and to the Industry Assistance Office (IAO/OTS/EPA) for appropriate distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0283-0470
Page 1 of 3

DATE: MAR 8 1983

SUBJECT: Status Report* 8EHQ-0283-0470

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Approved 3/14

Revision Needed ______

Submission Description

The Angus Chemical Company submitted complete copies of the final reports, including test protocols and data, from two in vitro genetic toxicity screening assays of 4,4-dimethyl-1,3-oxazolidine (CAS No. 51200-87-4). According to the submitted information, 4,4-dimethyl-1,3-oxazolidine caused a significant dose-dependent increase in the chromosomal aberration frequency in cultured Chinese Hamster Ovary (CHO) cells both in the presence and absence of exogenous metabolic activation. In addition, the subject chemical was reported to cause a dose-dependent mutagenic response both in the absence and presence of metabolic activation in cultured Mouse Lymphoma L5178Y TK+/- cells.

Submission Evaluation

The submitted data show that 4,4-dimethyl-1,3-oxazolidine induced a dose-related increase in chromosomal aberrations in CHO cells when tested both with and without metabolic activation. Although metabolic activation reduced cellular toxicity, it had no effect upon the chemical's ability to induce chromosomal aberrations. Both in the presence and absence of activation, the highest dose tested increased the number of aberrations per cell approximately 5X over that seen in the untreated control culture. In addition, the highest dose tested was as active as the positive control chemical for that particular assay (i.e., 0.11 ul/ml test agent was as active as 0.5 ug/ml triethylenemelamine in the assay without activation and 0.28 ul/ml test agent was as active as 35 ug/ml cyclophosphamide in the assay with activation).

The submitted data also show that 4,4-dimethyl-1,3-oxazolidine induced a dose-related increase in the number of TK locus mutations in a population of cultured mouse lymphoma L5178Y cells. Without metabolic activation, an increase in mutation frequency ranging from 2X to 18X that of the untreated control cultures was observed at test material concentrations of 0.010 ul/ml to 0.032 ul/ml. When tested with activation, concentrations of 0.075 ul/-ml and 0.10 ul/ml induced mutation frequencies of about 3X to 4X over that seen in the untreated control cultures. The metabolic activation also reduced both cellular toxicity and mutagenic potency. In the presence and absence of activation, the highest dose tested was approximately as active as the positive control compound (i.e., 0.032 ul/ml of test agent was approximately as active as 0.5 ul ethyl methanesulfonate in the assay without metabolic activation and 0.1 ul/ml was approximately as active as 5 ug/ml 7,12-dimethyl-benzanthracene in the assay with activation).

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Current Production and Use

A review of the production range (includes importation volumes) statistics for 4,4-dimethyl-1,3-oxazolidine (CAS No. 51200-87-4), which is listed in the initial TSCA Inventory, has shown that no 1977 production/importation was reported or that all of the production range data reported were claimed as confidential by the manufacturer(s) and/or importer(s) and cannot be disclosed (Section 14(a) of the Toxic Substances Control Act, U.S.C. 2613(a)). The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

Although the Angus Chemical Company's submission did not contain any information pertaining to the use(s) of 4,4-dimethyl-1,3-oxazolidine, the chemical is listed in the Third Edition (1982) of the Cosmetics, Toiletries, and Fragrances Association (CTFA) Cosmetics Ingredient Dictionary. No further information on the use(s) of the subject chemical was located in the secondary literature sources consulted.

Comments/Recommendations

It should be noted that although a positive *in vitro* result, when considered alone, may not be sufficient to offer reasonable support for a conclusion of substantial risk, EPA does believe that *in vitro* studies provide valuable data that can aid in assessing possible risks posed by chemicals to health and/or the environment. EPA also believes that positive *in vitro* test results in combination with additional information (e.g., knowledge of potential exposure to or high production of the chemical substance or mixture) would, in many cases, suggest the need for further more definitive toxicologic study with the results of such tests considered for possible submission pursuant to TSCA Section 8(e).

a) Considering the Agency's general interest in those company actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the Chemical Hazard Identification Branch (CHIB/AD/EPA) will request the

Angus Chemical Company to describe the voluntary actions it has taken in response to the submitted genotoxic data to warn workers and others and to reduce or eliminate exposure to 4,4-dimethyl-1,3-oxazolidine. The company will also be asked if it is conducting, or plans to conduct, further studies designed to better define the toxicity of the subject chemical. In addition, the Angus Chemical Company will be informed that EPA would welcome the submission of information pertaining to current production/-importation volumes, use(s), and worker, consumer, and environmental exposure to 4,4-dimethyl-1,3-oxazolidine.

b) The Chemical Hazard Identification Branch will screen the submitted information on 4,4-dimethyl-1,3-oxazolidine in order to determine if further OTS assessment is warranted.

c) The Chemical Hazard Identification Branch will transmit a copy of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, and ORD/EPA. In addition, copies will be sent to the Industry Assistance Office (IAO/OTS/EPA) and the Office of Toxics Integration (OTI/OPTS/EPA) for appropriate distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

Page 1 of 5

DATE: APR 4 1983

SUBJECT: Status Report* 8EHQ-0283-0471 S and
8EHQ-0383-0471 Supplement

Approved 4/5

Revision Needed ________

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Submission Description

In its initial submission, the Ferro Corporation notified EPA that the company had been recently informed by certain customers that several incidents of contact dermatitis had occurred among workers exposed to metalworking chemicals and products including Ferro's industrial lubricant additive product, Klarus 1717. In addition, the submitter reported that Klarus 1717 (major chemical component reported to be bis(2-chlorooctyl) disulfide; CAS No. 70776-26-0) had recently been found to exhibit "moderate to extreme potential to produce dermal sensitization in the guinea pig." In the initial submission, the Ferro Corporation also provided the summarized final results from several other acute *in vivo* toxicity and two *in vitro* genotoxicity tests of Klarus 1717

With regard to the reported incidents of contact dermatitis among metalworkers using lubricating fluids containing Klarus 1717, the Ferro Corporation stated that an informal investigation initially showed that "in each case, the worker involved used kerosene to wash parts and came into contact with the kerosene" and "other workers at the same sites who came into contact with lubricants containing Klarus 1717, but who did not come into contact with kerosene, did not develop any reported cases of contact dermatitis." In its supplemental submission, however, Ferro stated that further investigation indicated that "not every case of dermatitis alleged to be connected with metalworking fluids containing Klarus 1717 also involved exposure to kerosene." In addition, the submitter reported that "while it appears that all cases involved exposure to both a Klarus-containing fluid and a solvent degreaser, in some cases the solvent degreaser was 1,1,1-trichloroethane, in some it was stoddard solvent, and in some (most) cases it was kerosene."

With regard to the acute *in vivo* toxicity of Klarus 1717, the Ferro Corporation reported in the initial submission that Klarus 1717 was found to have an acute oral (rat) LD50 greater than 5.0 g/kg and an acute dermal (rabbit) LD50 greater than 2.0 g/kg.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

In addition, the submitter reported that Klarus 1717 "produced generally mild irritation persisting for seven days to the eyes of all animals [rabbits] and mild transient corneal opacity observed after fluorescein staining in the eyes of two of nine New Zealand white rabbits." With regard to the performed *in vitro* studies, it was reported that Klarus 1717 was non-mutagenic in Ames *Salmonella typhimurium* (bacteria) assays conducted in the presence and absence of exogenous metabolic activation. In a *Saccharomyces cerevisiae* (yeast) Mitotic Gene Conversion Assay, Klarus 1717 was reported to be mutagenic in the absence of exogenous metabolic activation and caused increased numbers of *S. cerevisiae* mutants in the presence of metabolic activation. According to the submitter, not all of the criteria for a positive test were met in the yeast assay conducted in the presence of metabolic activation.

Submission Evaluation

Based on the provided information, Klarus 1717 does appear to have only slight oral and dermal medium lethality. There was no indication in the submission that an acute inhalation LC50 study was performed on the product. Although the product was not found to be a severe eye irritant, in terms of irreversible eye tissue damage, it did cause (reversible) corneal opacity and effects persisted for seven (7) days. Such observations suggest that the eye irritancy of Klarus 1717 is not trivial.

Dermatitis (skin inflammation) can be the result of, among other things, the repeated defatting of the skin by frequent dermal contact with various chemicals. Dermal exposure to kerosene and/or other solvents probably plays more of a role in additive defatting (thereby facilitating absorption of other chemicals through the skin) than in the actual induction of sensitization reactions (e.g., contact dermatitis).

Contact dermatitis is a delayed type of induced allergy of the skin with varying degrees of redness, swelling, and blistering resulting from dermal contact with a specific antigen. Chemical substances and/or their metabolites can be antigenic on the basis of their molecular structure and can also combine with endogenous proteins in the body to form antigenic complexes. Allergic reactions are of concern because they 1) can be evoked in response to a small amount of antigen, 2) can be manifested at or around the site of exposure and/or away from the site of exposure, 3) can range in intensity from mild to severe, and 4) can be evoked upon exposure to other antigens (cross-reactivity). In some cases, allergic reactions can be life-threatening should they involve symptoms such as swelling in the tissues of the respiratory tract. In the absence of specific evidence (e.g., bronchial constriction), however, there is no basis to conclude that a substance that can induce dermal sensitization will also induce asthmatic or anaphylactic-type sensitization reactions.

Integumentary (skin) hazard is judged by at least four criteria: 1) degree or intensity of effect, 2) reversibility of effect, 3) duration of effect, and 4) incidence of the observed effect among those exposed. Intensity would include the continuum from no effect through redness and edema to corrosion and scarring to, ultimately, lethality. The classification of dermal sensitizers is based upon incidence rather than intensity in that a "potent" dermal sensitizer will affect a substantial fraction (though not necessarily a majority) of those exposed, although the individual reactions may range from relatively mild to severe. It should be noted that dermatitis is not necessarily a sensitization reaction as it is possible to find both responses in the same individual at the same time. It should also be noted that irritation, which usually occurs early following exposure to an irritant, can be prolonged and may in some cases seem to have a latent period. Dermal sensitization reactions, on the other hand, may not develop until several days have elapsed since exposure to the causative agent(s); asthmatic or anaphylactic-type sensitization reactions can occur promptly (usually within an hour or two following exposure). There is, therefore, some overlap in time of onset between the effects of sensitizers having an early onset and irritants having a late onset. This overlap may, in some cases, hinder the diagnosis of dermal ailments and attempts to determine their causative agent(s).

In view of the above discussion, and considering 1) the laboratory evidence that Klarus 1717 exhibited "moderate to extreme potential to produce dermal sentization in guinea pigs," 2) the fact that certain metalworkers are exposed to Klarus 1717, and 3) the preliminary evidence that the reported incidents of contact dermatitis occurred among workers exposed to Klarus 1717 and other metalworking chemicals, the possibility that Klarus 1717 may be the (or one of the) causative agent(s) should be investigated further. Such an investigation is now being conducted by the Ferro Corporation.

In order for EPA to evaluate more properly the reported toxicity information, the Ferro Corporation should be requested to provide a complete copy of the final report (including test protocol(s) and data) from each of the *in vitro* and *in vivo* studies cited in the company's initial submission.

Current Production and Use

A review of the production range (includes importation volumes) statistics for bis(2-chlorooctyl) disulfide (CAS No. 70776-26-0), which is listed in the initial TSCA Inventory, has shown that between 100 thousand and 1 million pounds of the subject chemical were reported as produced and/or imported in 1977. This production range information does not include any production/importation data claimed as confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information that would compromise Confidential Business Information. The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

In general, metalworking fluids (also known as cutting/grinding fluids) are applied to cutting tools to aid in machine operation by serving as lubricants and/or coolants and by washing away metal chips. Although the Ferro Corporation reported that bis(2-chlorooctyl) disulfide was the major component of Klarus 1717, the submitter did not provide any information concerning the identity and amount of the other chemical constituent(s) of subject lubricant additive product.

Comments/Recommendations

In its supplemental submission, the Ferro Corporation stated that the company is in the process of transmitting copies of the submitted information to each Klarus 1717 customer and to persons who have received research samples of the product. In addition, the submitter stated that an investigation of the reported incidents of contact dermatitis is continuing and that EPA will be advised of any significant conclusions that are reached.

With regard to in vitro genotoxicity studies, EPA believes that such studies provide valuable data that can aid in assessing possible hazards/risks posed by chemical substances or mixtures to health and/or the environment. In addition, EPA believes that positive in vitro test results in combination with additional information (e.g., knowledge of high production/importation of and/or potential for exposure to the chemical substance or mixture) would, in many cases, suggest the need for further more definitive toxicologic study with the results of such testing considered for possible submission to EPA pursuant to Section 8(e) of TSCA.

EPA's Office of Toxic Substances (OTS) has received and evaluated several TSCA Section 8(e) and "For Your Information (FYI)" submissions concerning the toxicity of and/or exposure to cutting fluids, kerosene, stoddard solvent, and 1,1,1-trichloroethane. In addition, the Chemical Hazard Identification Branch (CHIB/AD/-OTS) has prepared a Chemical Hazard Information Profile (CHIP) on cutting fluids. At present, the OTS "Existing Chemicals Task Force (ECTF)" is reviewing toxicity and exposure data on cutting fluids and the Test Rules Development Branch (TRDB/AD/OTS) is reviewing toxicity and exposure data on 1,1,1-trichloroethane.

a) The Chemical Hazard Identification Branch will request the Ferro Corporation to provide information pertaining to the exact identity and amount of each chemical constituent (including known contaminants) of Klarus 1717. In view of EPA's general interest in voluntary corporate actions taken in response to chemical toxicity/exposure information, the Ferro Corporation will be asked if it is conducting, or plans to conduct, any further laboratory studies (e.g., mammalian cell genotoxicity) designed to define better the toxicity of Klarus 1717 and/or the chemical components of Klarus 1717.

b) The Chemical Hazard Identification Branch will transmit copies of this status report to NIOSH, OSHA, CPSC, NTP, OW/EPA, OSWER/EPA, OANR/EPA, ORD/EPA, TRDB/AD/EPA, and the "Existing Chemicals Task Force (ECTF)." In addition, copies of this status report will be provided to the Industry Assistance Office (IAO/OTS/EPA) and the Office of Toxics Integration (OTI/OPTS/EPA) for appropriate distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0283-0472 S
Page 1 of 3

DATE: FEB 28 1983

SUBJECT: Status Report* 8EHQ-0283-0472 S

Approved 3/1/83

FROM: Justine L. Welch, JW Team Leader
Chemical Selection and Profiles Team/CHIB

Revision Needed ____________

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Submission Description (See NOTE on Page 3 of this status report)

The submitting company (company name claimed as Confidential Business Information (CBI)) provided summarized preliminary results from a lifetime mouse skin-painting study of heavy catalytic reformed petroleum naphtha (CAS No. 64741-68-0) both alone and admixed 3:1 with kerosene (CAS No. 8008-20-6). According to the submitter, fifty (50) microliters of the materials were applied directly to the skin of the back of fifty (50) male mice, two (2) times per week for the lifetime of the mice.

With regard to those mice treated with heavy catalytic reformed naphtha alone, the submitter reported that:

> "Two mice developed one tissue mass each at the application site, with a mean latency period of 67.5 weeks. Histopathology examinations of these masses has not yet been done. Masses not located at the site of application occurred in 28 animals. These are not considered to be treatment related as such masses occurred in 41 and 45 animals in the 2 control groups which were run with the study."

For those mice treated with the 3:1 heavy catalytic reformed naphtha/kerosene mixture, the submitter reported that:

> "Five mice developed one mass each at the site of application, with a mean latency period of 95.8 weeks. Based on gross observations, [the performing laboratory] reports two benign tumors and three advanced tumors. Histopathology for these masses is not yet completed and therefore it is not known whether malignant tumors were present."

With regard to the reported preliminary results, the submitting company stated that "although the long latency period and the small number of tumors indicates that the [tested materials] are weak animal carcinogens," the company believes that the materials "are not likely to present a carcinogenic risk to employees or

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***NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.**

users." The submitter also stated that due to the fact that the tested materials are "skin irritants causing dryness and dermatitis upon prolonged exposure, both employees and customers avoid skin contact to prevent these acute effects." Finally, the submitter reported that prolonged skin contact to the materials is not a normal occurrence in that exposure in the workplace is "minimized by standard industrial hygiene control measures and good work practices."

Submission Evaluation (See NOTE on Page 3 of this status report)

Although the submitted preliminary information suggests that the heavy catalytic reformed petroleum naphtha when tested alone or admixed 3:1 with kerosene does possess some degree of oncogenic activity toward mouse skin, this observation is clouded by the apparent 80% and 90% incidences of non-application site masses (tumors?) reportedly found in the two control groups. It would not be surprising, however, that the tested material is oncogenic in light of the likely presence of polynuclear aromatic hydrocarbons. A complete copy of the final report from this study should be obtained in order for the Agency to evaluate more properly the reported toxicologic findings.

Current Production and Use (See NOTE on Page 3 of this status report)

According to the TSCA Chemical Substances Inventory, heavy catalytic reformed petroleum naphtha (CAS No. 64741-68-0) is defined as a "complex combination of hydrocarbons produced from the distillation of products from a catalytic reforming process. It consists of predominantly aromatic hydrocarbons having carbon numbers predominantly in the range of C7 through C12 and boiling in the range of approximately 90°C to 230°C (194°F to 446°F)."

A review of the production range (includes importation volumes) statistics for heavy catalytic reformed petroleum naphtha (CAS No. 64741-68-0), which is listed in the initial TSCA Inventory, has shown that over 60 billion pounds were reported as produced/-imported in 1977. **/

**/ This production range information does not include any production/importation data claimed as confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information which would compromise Confidential Business Information. The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

Comments/Recommendations

EPA's Office of Toxic Substances (OTS) has received and evaluated many TSCA Section 8(e) and "For Your Information (FYI)" submissions pertaining to the toxicologic properties of and/or exposure to various petroleum refinery process streams.

a) The Chemical Hazard Identification Branch (CHIB/AD) will request the submitter to provide, when available, a complete copy of the final report (including protocol(s) and histopathology data) from the subject lifetime mouse skin-painting study of heavy catalytic reformed naphtha.

b) The Chemical Hazard Identification Branch will screen the reported information to determine if further OTS assessment of heavy catalytic reformed petroleum naphtha is warranted.

c) The Chemical Hazard Identification Branch will transmit a copy of this status report to NIOSH, OSHA, CPSC, DOE, OW/EPA, OSWER/EPA, OANR/EPA, ORD/EPA, and to the EPA's "Alternate Fuels Workgroup." A copy of this status report will also be provided to the Office of Toxics Integration (OTI/OPTS/EPA) and to the Industry Assistance Office (IAO/OTS/EPA) for appropriate distribution.

NOTE: In a supplemental submission dated January 30, 1985, (8EHQ-0285-0472 S Supplement), the submitting company reported that the test material that was identified in the initial Section 8(e) submission as a heavy catalytic reformed petroleum naphtha (CAS No. 64741-68-0) could be more accurately described as a low-boiling catalytic reformer fractionator residue petroleum distillate (CAS No. 68477-31-6).

A review of the production range (includes importation volumes) statistics for CAS No. 68477-31-6, which is listed in the initial TSCA Inventory, has shown that between 10 thousand and 100 thousand pounds of this material were reported as produced/imported in 1977. This production range information does not include any production or importation data that were claimed as TSCA Confidential Business Information (TSCA CBI) by those person(s) reporting for the TSCA Inventory, nor does it contain any data that would compromise TSCA CBI. The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

2/12/85

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0383-0473
Page 1 of 5

DATE: APR 20 1983

SUBJECT: Status Report* 8EHQ-0383-0473

Approved 4/25

Revision Needed ______

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Submission Description

W. R. Grace & Co. (Grace) provided preliminary results of an ongoing company epidemiology study of past/present workers at the Grace vermiculite mining and milling operation in Libby, Montana. According to the submitter, the Libby vermiculite deposit has been long known to be contaminated with tremolite, an asbestiform material. W. R. Grace & Co. also reported that in addition to its own epidemiology study, the "National Institute for Occupational Safety and Health (NIOSH), acting at the request of the Mine Safety and Health Administration (MSHA), began a study in March 1982 of the effects of tremolite exposure upon present and past employees at Libby." The submitter stated that the NIOSH study is a "cooperative effort" and stated further that Grace has made its data available to NIOSH. The submitting company also reported that it has "developed estimates of historical individual worker exposure levels" and has recently started to compile other employee data with these estimates of individual worker exposure levels. In addition, W. R. Grace & Co. reported that NIOSH is now in the process of developing its own exposure estimates so that NIOSH and the company will be able to use the other's estimates for cross-comparison purposes, an activity which Grace hopes will "provide a more precise final product."

In its submission, W. R. Grace & Co. reported that the Libby vermiculite mining and milling facility, which has been in operation since the 1930's, was purchased by Grace in 1963 and currently employs 170 people. The submitting company stated that although "dust exposure levels" at Libby were "very high" prior to 1963, "conditions gradually improved" following the company's acquisition of the operation. The submitter also reported that a 1971 study (conducted by the U. S. Bureau of Mines) showed fiber exposures at Libby ranging from 13 to 71 fibers/cubic centimeter (cc) of air. W. R. Grace & Co. stated, however, that following "time-consuming research" in overcoming unique technical design problems, "a new wet milling facility was placed into operation [in 1974] followed by further major process and operational improvements in the mine, mill and other areas which improved working conditions significantly." The submitting company also reported that since 1974/1975, fiber "exposures have been dramatically lowered and at present average less than 0.2 fibers/cc (0.01-0.9 fibers/cc range)."

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

With regard to the preliminary results of its own ongoing study, W. R. Grace & Co. reported that the company's "information indicates that of 109 known deaths of former Libby employees, the cause of death for 16 was listed in death certificates or insurance claim forms as lung cancer, and for two others the cause was listed as mesothelioma." The company stated that it did not have "sufficient medical information or sufficient occupational and personal history data in these cases to make a judgment as to the cause of these illnesses." The submitting company also reported that based upon "individual exposure estimates, it appears that certain [Grace] employees whose work history predates the new mill and who have a cumulative exposure of less than 100 fiber years show signs of asbestos-related disease" and that "all of these employees had exposure levels of more than 2.0 fibers per cc for varying periods of time prior to the new mill."

W. R. Grace & Co. pointed out "several methodological problems which have prevented [the company] from making any preliminary judgments" based on the reported preliminary information. First, the company pointed out that the information pertains to conditions which "do not exist in today's workplace environment" and that "all of the employees who show signs of asbestos-related disease were employed prior to 1976 when fiber levels were significantly higher than they are today." The company noted that in contrast, its "preliminary data [show that] none of the current employees hired since 1975 have asbestos-related disease." Second, the company pointed out that "there are those who question the validity of using cumulative exposures (averaging periods of significantly high exposure with later low exposure periods) and the fiber year concept as a proper basis for evaluating the effects of asbestiform material exposure." Finally, the company pointed out that "the Libby employee population has a history of both a large number of smokers (about 75%) and relatively heavy individual smoking histories (most employees smoked a pack or more per day)."

W. R. Grace & Co. stated the company believes that the submitted preliminary information "corroborates written scientific opinion on the effects of exposure to asbestiform material and that it is within the realm of expectation for a mining and milling population having exposures at the levels which prevailed at Libby in the past." In addition, the submitting company stated that "in some respects, the data are similar to what has been reported in studies of talc mining and milling operations in which the talc contained tremolite and other forms of asbestos." Finally, Grace stated that "despite the uncertainty as to the meaning of the data," the company had submitted the subject preliminary findings pursuant to Section 8(e) for the following reasons: "(1) the expressed interest of EPA, NIOSH, OSHA and MSHA in determining whether the various asbestiform materials induce different medical effects, and (2) ongoing agency investigations as to whether current asbestos exposure standards are adequate."

Submission Evaluation

It is agreed that the reported serious health effects (i.e., 16 lung cancers/109 deaths and 2 mesotheliomas/109 deaths) are corroborative of written scientific opinion on the effects of exposure to asbestiform materials and that the effects are, as the submitter stated, "within the realm of expectation for a mining and milling population having exposures at the levels which prevailed...in the past."

In the submitter's study cohort, the proportion of men having smoked was estimated to be 75%, a figure that is consistent with other estimates of the proportion of males who have smoked in the past.(1) For lung cancer, the estimated probability of death due to lung cancer in males in the U.S. from age 35 until age 74 is .062 or 6.2%.(2) Because this was a working population, it is assumed that the deaths due to lung cancer did not occur before age 35 and the population was followed to at least age 74. The observed proportion of deaths due to lung cancer was 16/109 or .147 (14.7%). Therefore, the calculated relative risk would be approximately 2.4, which is statistically significant at $p < 0.01$ and is consonant with the known synergistic effects of asbestos in smokers.

For mesothelioma, there is no established background incidence for this disease. However, the rate estimates for asbestos-related mesothelioma in North America in the mid-1970's were $8.0/10^6$ for males and about $2.5/10^6$ for females.(3) If the incidence of mesothelioma observed in the deceased Libby employees (i.e., 2 mesotheliomas/109 deaths) is projected to a population of 10^6, the rate would be equivalent to 18,349 cases of mesothelioma. This finding is quite significant even though the exposure levels between the two groups (i.e., the North American males/females versus the studied Libby population) are not comparable. In addition, the finding is not necessarily surprising in light of the 13-71 fibers/cc found by the U.S. Bureau of Mines during the 1971 survey of the Libby facility. In addition, W. R. Grace & Co. stated in the submission that exposure levels at the Libby operation were even higher prior to 1970.

It would be of interest to know the actual past/present exposure levels for the current Libby employees who reportedly show signs of asbestos-related disease(s), the number of current employees affected, and the nature of the asbestos-related disease(s) that are occurring. In addition, it should be noted that the submitter's finding that none of the current employees hired since 1975 show signs of asbestos-related disease is not surprising because inadequate time has passed for the potential asbestos-related diseases to be significantly expressed.

The submitter's final comment that W. R. Grace & Co. has "no reason to believe there is any risk associated with the current uses of Libby vermiculite-containing products" remains to be determined and is dependent upon the potential exposure of users to asbestos from the Libby vermiculite-containing products and the inherent risk such uses impose.

Current Production and Use

Vermiculite is a naturally occurring hydrated magnesium-iron-aluminum silicate (CAS No. 1318-00-9) that when heated (2000°F) can expand (exfoliate) from 6-20 times its original size. The known major vermiculite deposits are located in South Africa, Wyoming, Colorado, Montana, North Carolina, and South Carolina. Vermiculite uses include: insulating and packing materials; filler for paints, plastics, and rubber; removal of strontium-90 from milk and phosphates from wastewater; animal feed and fertilizer additive; insecticide carrier; plant bedding; and general absorbant.

Tremolite (CAS No. 14567-73-3) is a variety of asbestos which is used particularly in paints, ceramics, and acid-resisting applications.

Comments/Recommendations

W. R. Grace & Co. reported that its medical surveillance program at the Libby facility includes annual chest X-rays (since 1964), annual pulmonary function tests (since 1974), and health status questionnaires (since 1978). The company stated that the results of these tests are made available to individual Libby employees and/or their personal physicians. In addition, the company reported that "based upon the recognition that smoking and asbestos exposure can increase the incidence of disease, Grace, in 1978, banned smoking at all Company facilities in Libby." W. R. Grace & Co. also reported that it has initiated a program designed to "help employees stop smoking, and the smoking population has been reduced to 25% of the staff." In addition, the company stated that "all new hires are required to be nonsmokers." W. R. Grace & Co. reported that because of the difficulties in interpreting the submitted information, the company plans to retain Drs. J. C. McDonald and A. D. McDonald (McGill University, Montreal, Canada) to "undertake a thorough analysis of the Libby data" in order to allow Grace "to reach a scientifically sound conclusion based upon [the company's] historical data." W. R. Grace & Co. also reported that the company does plan to continue to cooperate with NIOSH and has sent a copy of the company's 8(e) notice to NIOSH.

The National Toxicology Program (NTP) recently completed a lifetime carcinogenesis bioassay of blocky (nonfibrous) tremolite administered at a 1% concentration in the pelleted diet of male and female Fischer 344 rats (starting with the dams of the test animals). According to the DRAFT NTP Technical Report, "Under the conditions of this bioassay, nonfibrous tremolite was not toxic and did not cause a carcinogenic response when ingested at a level of 1% in the diet of male and female Fischer 344 rats for their lifetime."

a) The Chemical Hazard Identification Branch (CHIB/AD/EPA) will request W. R. Grace & Co. to report the actual past and present exposure levels for the Libby employees who are reportedly experiencing asbestos-related disease(s), the number of employees affected by such disease(s), and the nature of those asbestos-related disease(s). The company will also be requested to submit, when available, a complete copy of the results (including methodologies and data) of the Libby data analysis which is to be performed by Dr. A. D. McDonald and Dr. J. C. McDonald at McGill University in Montreal, Canada.

b) The Chemical Hazard Identification Branch will provide copies of this status report to NIOSH, OSHA, CPSC, MSHA, OW/EPA, OSWER/EPA, OANR/EPA, CRD/EPA, and the "Asbestos Team" (CCD/OTS/EPA). Copies of this status report will also be transmitted to the Industry Assistance Office (IAO/OTS/EPA) for appropriate distribution.

References

1 Preventive Medicine. 1980. Vol. 9, pp. 747-759.

2 SEER Report, NCI Monograph 57, June 1981.

3 McDonald JC and McDonald AD. Mesothelioma as an index of asbestos impact. In: Peto R, Schneiderman M (ed), Banbury Report 9, Quantification of Occupational Cancer, Cold Spring Harbor Laboratory, 1981, pg. 73-82.

NOTE:

In a supplemental submission dated June 7, 1983 (8EHQ-0683-0473 Supplement), R. T. Vanderbilt Company, Inc. reported that the asbestiform (i.e., fibrous) variety of tremolite is correctly termed "tremolite asbestos" (CAS No. 77536-68-6), whereas the non-fibrous (i.e., non-asbestiform) variety is correctly termed "tremolite" (CAS No. 14567-73-8).

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0383-0474
Page 1 of 4

DATE: APR 25 1983

SUBJECT: Status Report* 8EHQ-0383-0474

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Approved 4/26

Revision Needed ______

Submission Description

The Celanese Corporation provided the experimental protocol and a "poster" summarizing the preliminary findings from the first 15 months of an ongoing chronic rat inhalation study of acetaldehyde (CAS No. 75-07-0) which is being conducted in the Netherlands. Celanese also provided a January 6, 1983 cover letter from the Institute CIVO - Toxicology and Nutrition TNO (Netherlands) to the National (U.S.) Center for Toxicological Research (NCTR) and one of that letter's two enclosures (an NCTR/EPA Formaldehyde Clearing House Data Form on acetaldehyde). The other enclosure (a Data Form on formaldehyde) was not included in the submission.

According to the submitted acetaldehyde Data Form, the Institute CIVO - Toxicology and Nutrition TNO, the Netherlands Ministry of Health and Environment, and the Netherlands Cancer Foundation are co-sponsors of the subject study ("Lifespan Inhalation Carcinogenicity Study of Acetaldehyde in Rats"). The January 6, 1983, cover letter states that the chronic inhalation study and several short-term inhalation studies in rats were initiated to verify previously reported oncogenic effects of acetaldehyde in Syrian Golden hamsters following long-term inhalation exposure. The short-term studies in rats reportedly revealed "severe degenerative, hyperplastic and metaplastic epithelial changes in the nose at levels of 1000, 2200, and 5000 ppm; similar changes were also found in the larynx at the two highest exposure levels."

According to the "poster" summary, the ongoing chronic study, which has been underway for 21 months as of January, 1983, involves 4 groups of Wistar rats, each group consisting of 105 males and 105 females, exposed via inhalation to acetaldehyde vapor concentrations of 0, 750, 1500, or 3000 parts per million (ppm) for 6 hours per day, 5 days per week for at most 30 months. The "poster" summary stated that interim sacrifices have been carried out at 3, 6, and 12 months and further stated that "recovery groups" have been included in the study.

***NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.**

With regard to the preliminary results of the ongoing chronic acetaldehyde inhalation study in rats, the submitted "poster" summary stated that:

> "Mortality was significantly increased in males and females of the top-dose group as compared to controls. Growth retardation was observed in males at each treatment level and in females at the mid- and top-dose levels. The histopathological examination of rats killed after 3, 6, or 12 months revealed hyper- and metaplastic epithelium with massive keratini[z]ation in the nose, and similar, but less severe changes in the larynx at the highest exposure level. Less severe degenerative and hyper/metaplastic changes in the nose were also found at the lower exposure levels. The first nasal carcinoma (a squamous cell carcinoma from the respiratory epithelium) was found in a top-dose rat in week 44. A considerable number of top-dose rats found dead or killed in extremis during the first 15 months of the study had a nasal carcinoma (7/35 males and 13/31 females). Both squamous cell carcinomas and adenocarcinomas of the olfactory epithelium were observed. A few lower dose rats had also developed a nasal carcinoma. So far, no laryngeal tumors were detected."

The "poster" summary also contains the following conclusion:

> "It is concluded that under the conditions of the present study, acetaldehyde is capable of inducing nasal carcinomas in rats."

In addition, the submitted January 6, 1983, cover letter discussed the possible role of cytotoxicity in both formaldehyde and acetaldehyde carcinogenicity and the perceived need for further study. The cover letter also addressed the question of risk of human lung and laryngeal cancer posed by exposure to formaldehyde and/or acetaldehyde.

Submission Evaluation

The submitted summary information clearly indicates that inhaled acetaldehyde vapors are carcinogenic toward the respiratory tract of rats. The provided information also indicates the existence of a dose-response relationship. Further evaluation of the reported carcinogenic findings in rats will be possible upon EPA's receipt of future interim reports as well as a complete copy of the final report (expected in the summer of 1984).

Current Production and Use

A review of the production range (includes importation volumes) statistics for acetaldehyde (CAS No. 75-07-0), which is listed in the initial TSCA Inventory, shows that between 771 million and 2.2 billion pounds of this chemical were reported as produced and/or imported in 1977. This production range information does not include any production/importation data claimed confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information that would compromise Confidential Business Information. The data submitted for the initial TSCA Inventory, including production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

The major use of acetaldehyde is as an intermediate in the manufacture of a wide variety of chemical substances (e.g., acetic acid and peracetic acid, pyridine and pyridine bases, pentaerythritol, glyoxal, 1,3-butylene glycol, paraldehydes, acetic anhydride, butyl alcohol, butyraldehyde, chloral). In addition, acetaldehyde is used to manufacture perfumes, polyester resins, and basic dyes. The chemical has also been used as a fruit and fish preservative, as an alcohol denaturant, as an additive in certain foodstuffs and alcoholic beverages, and as a solvent in the paper, rubber, and tanning industries. Some of the other applications of acetaldehyde include its use in fuel compositions, in preventing mold growth on leather goods, in silvering of mirrors, and in producing certain types of thermoset resins.

Comments/Recommendations

The Celanese Corporation's submission indicated that the company had provided copies of the reported information to NIOSH, OSHA, and NCI. In addition, Celanese has reported that the company is attempting to obtain additional information from the laboratory investigators and plans to forward that information to EPA. The provided NCTR/EPA Data Form on acetaldehyde indicates that the projected date for the final report of the chonic inhalation study in rats is July, 1984.

The Chemical Hazard Identification Branch (CHIB/AD) is currently preparing a Chemical Hazard Information Profile (CHIP) on acetaldehyde. In addition, the National Toxicology Program has been conducting other toxicologic studies of the subject chemical.

a) The Chemical Hazard Identification Branch (CHIB/AD/EPA) will request the Celanese Corporation to immediately submit (upon receipt by the company) copies of all future interim reports and a copy of the final report from the ongoing chronic acetaldehyde inhalation study in rats. In view of EPA's general interest in corporate actions which are taken on a voluntary basis in response to chemical toxicity/exposure information, Celanese will be requested to describe the actions it has taken to warn workers and to reduce and/or eliminate exposure to acetaldehyde.

b) The Chemical Hazard Identification Branch will ensure that the oncogenicity findings in rats are incorporated in the acetaldehyde Chemical Hazard Information Profile (CHIP) which is now in preparation.

c) The Chemical Hazard Identification Branch will transmit copies of this status report to NIOSH, OSHA, FDA, CPSC, NTP, OW/EPA, OSWER/EPA, OANR/EPA, ORD/EPA, and OPP/EPA. Copies of this status report will also be sent to the Industry Assistance Office (IAO/OTS/OPTS) for additional distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0483-0475
Page 1 of 4

DATE: APR 29 1983

SUBJECT: Status Report* 8EHQ-0483-0475

Approved 5/3

Revision Needed

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Submission Description

The Eastman Kodak Company submitted a March 2, 1983, interim summary report entitled "Inhalation Teratological Potential of Ethylene Glycol Monobutyl Ether [EGBE; 2-butoxyethanol] in the Rat." Eastman Kodak reported that the study is being conducted under contract for the Chemical Manufactures Association (CMA) and is being sponsored by the Glycol Ether Program (GEP) of which the Tennessee Eastman Company (a division of the Eastman Kodak Company) is a member. In its submission, Eastman Kodak noted that the data contained in the interim report "have not been subjected to Quality Assurance and are incomplete since fetal skeletal examination and statistics have not been finished."

According to the submitted interim report, 4 groups of 30 mated female Fischer 344 rats were exposed via inhalation to EGBE vapor concentrations of 0, 100, 200, or 300 ppm for 6 hours per day on gestation days (GD) 6 through 15. In addition, the interim report presented the following summarized clinical observations and results of examinations performed as of March 2, 1983:

> "Gestation Body Weight Changes: Gestational body weight gains of animals exposed to 300 ppm were significantly depressed (compared to controls) from GD 6-21. Significant reductions in body weight gains (compared to controls) were also present in the 200 ppm group from GD 6-15 and in the 100 ppm group from GD 6-12."
>
> Gestational Food Consumption: Food consumption was reduced during the dosing period in all groups exposed to EGBE. Significant reductions in food consumption (compared to controls) were noted in the 300 ppm group from GD 6-15, in the 200 ppm group from GD 6-12, and in the 100 ppm group from GD 6-12. Animals in the 300 and 200 ppm groups had a significant increase in their food consumption (compared to controls) from the end of exposures (GD 15) until sacrifce (GD 21).

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Gestational Water Consumption: Only animals exposed to 300 and 200 ppm had significant reductions in water consumption. Those exposed to 300 ppm consumed less water than controls from GD 6-12. Animals in the 200 ppm group consumed less water than controls in the periods GD 6-9 and GD 12-15. Water consumption prior to the exposure segment of the study and following exposures were similar in all groups.

Maternal Clinical Observations: Exposures to EGBE resulted in a dose-related increase in the frequency of signs indicative of hematuria. These signs included red fluid on cage trays, and urogenital wetness, discharges and encrustations of red and/or black color. In addition, animals exposed to EGBE were hypoactive during the exposure segment of the study when compared with controls.

Maternal Organ Weights: The weight of the uteri of animals exposed to 300 ppm was significantly lower than those of controls. This reduction in uterine weight is associated with the high degree of embryo and fetal lethality present at this exposure level.

Maternal Uterine and Ovarian Examinations: Exposures to EGBE, particularly at the 300 ppm level, resulted in a marked increase in embryo and fetal lethality manifested by resorptions of concepti. Exposures to 200 ppm produced a more moderate increase in resorption when compared to controls.

Fetal Visceral Examinations: Exposures to EGBE resulted in a dose-related increase in fetal atelectasis [the incomplete expansion of the lung(s) at birth]. In addition, fetuses from groups exposed to EGBE had ventricular septal defects, absent innominate arteries, and severely shortened innominate arteries."

In addition to the March 2, 1983, interim report, the Eastman Kodak Company provided the following background information:

"Nelson et al at the National Institute for Occupational Safety and Health (NIOSH) studied the teratogenic potential of three glycol ethers in rats; 2-butoxyethanol (EB), 2-methoxyethanol (EM), and 2-ethoxyethyl acetate (EEA). They found that EM and EEA were teratogenic, while 2-butoxyethanol did not produce significant embryofetotoxicity. The exposure concentrations of 2-butoxyethanol were 150 to 200 ppm and Nelson et al reported that these concentrations were difficult to generate (vapor pressure of EB = 0.6 mm Hg at 20°C). Maternal toxicity was evident at both dose levels and consisted of hematuria only after the first exposure. No other adverse effects were seen in the dams exposed to either level. No major skeletal or soft tissue malformations were seen at 150 or 200 ppm of 2-butoxyethanol and the incidence of common skeletal variants and minor soft tissue anomalies seen in the treated groups were comparable to the controls. Potential

> reproductive effects of 2-butoxyethanol and other glycol ethers were studied in male rats in [the submitter's] laboratory and in male mice by Nagano et al in Japan. Administration was by gavage five times per week. In the former, doses from 222 to 885 mg/kg/day, and in the latter, doses from 250 to 1000 mg/kg/day, did not produce testicular effects."

Finally, Eastman Kodak noted that the following factors should be considered by EPA in assessing the CMA/GEP-sponsored inhalation teratology study of 2-butoxyethanol in rats: "the severe maternal toxicity produced, the lack of a dose-related response and the low incidence of effects seen in the [CMA/GEP] study, as well as the negative results from the NIOSH study, the known toxicity of 2-butoxyethanol in adult male and non-pregnant female rats, and [the chemical's] vapor pressure."

Submission Evaluation

Although the submitted findings indicate that 2-butoxyethanol did produce some degree of maternal toxicity in the CMA/GEP-sponsored teratology study, EPA does not believe that 2-butoxyethanol produced "severe" maternal toxicity in the study. One of the most common major manifestations of severe maternal toxicity in this type of study is a significant weight change (usually seen as a decrease) in exposed versus control dams. The summarized data that are presented in Table 4 (which contains measured maternal organ weights and "corrected" maternal body weights (i.e., the maternal body weight minus the weight of the uterus and its contents)), indicate that there were no significant changes in the corrected body weights of exposed dams when compared to the corrected body weights of control dams. There was, however, a significant decrease found in the uterine weights of dams exposed to 300 ppm 2-butoxyethanol when compared to controls. Stated in another way, the apparent decreases in maternal body weights of dams exposed to 300 ppm 2-butoxyethanol are due primarily to the decrease in the weight of the uterus and its contents.

In order for EPA to more properly evaluate the significance of the embryo/fetotoxic effects (including abnormalities) observed in the CMA/GEP-sponsored inhalation study of 2-butoxyethanol, a complete copy of the final report (including protocol(s), data and the results of performed statistical analyses) should be obtained. It should be noted at the present time, however, that the embryo/fetotoxic effects observed in the CMA/GEP-sponsored study (although in apparent contrast to previous findings), are consistent with the adverse developmental effects found in laboratory animals exposed to two structurally related chemicals: 2-methoxyethanol and 2-ethoxyethanol.

Current Production and Use

A review of the production range (includes importation volumes) statistics for 2-butoxyethanol (CAS No. 111-76-2), which is listed in the initial TSCA Inventory, has shown that between 31 million and 161 million pounds of this chemical were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed as confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information which would compromise Confidential Business Information (CBI). The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

2-Butoxyethanol is used as a solvent for nitrocellulose resins, spray and quick-drying lacquers, varnish and varnish removers, enamels, and drycleaning compounds. The chemical is also used for preventing spotting during the printing and/or dyeing of textiles and as an ingredient in certain pesticides.

Comments/Recommendations

EPA's Office of Toxic Substances (OTS) has received and evaluated several Section 8(e) and "For Your Information (FYI)" submissions concerning various glycol ethers. The Chemical Hazard Identification Branch (CHIB/AD/OTS) has prepared CHIPs (Chemical Hazard Information Profiles) on 2-methoxyethanol, 2-ethoxyethanol, and their acetates. In addition, Priority Review Level-1 (PRL-1) documents on 2-methoxyethanol and 2-ethoxyethanol have been prepared by the Health and Environmental Review Division (HERD/OTS). At present, the OTS "Existing Chemicals Task Force (ECTF)" is considering various EPA options with regard to chemicals within the class of glycol ethers.

a) The Chemical Hazard Identification Branch will request the Eastman Kodak Company to submit, when available, a complete copy of the final report from the CMA/GEP-sponsored inhalation teratology study of 2-butoxyethanol in rats. The submitter will also be requested to provide a complete copy of the final report (including test protocols and data) from the Eastman Kodak study reportedly conducted to determine potential reproductive system effects of 2-butoxyethanol administered to male rats by gavage five (5) times per week at doses ranging from 222 to 885 mg/kg/day.

b) In view of EPA's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the Chemical Hazard Identification Branch will request the Eastman Kodak Company to describe the actions it has taken to warn workers and others and to reduce and/or eliminate exposure to 2-butoxyethanol.

c) The Chemical Hazard Identification Branch will transmit a copy of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OANR/EPA, ORD/EPA, OSWER/EPA, OW/EPA, OPP/OPTS/EPA, and the OTS "Existing Chemicals Task Force (ECTF)." A copy of this report will also be provided to EPA's Industry Assistance Office (IAO/OTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0483-0476 S
Page 1 of 4

DATE: MAY 2 1983

SUBJECT: Status Report* 8EHQ-0483-0476 S

Approved 5/4

Revision Needed

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Submission Description

Note: The identity of the submitting company has been claimed as Confidential Business Information (CBI).

The submitting company provided summary results of two recently conducted genotoxicity studies of hexafluoroisobutylene (HFIB; CAS No. 382-10-5). The submitter reported that in the first study, sex-linked recessive lethal mutations were observed in fruit flies (Drosophila melanogaster) following a 2-hour exposure to HFIB at a concentration of 10,000 ppm (vol/vol). The second study reportedly involved rabbits exposed via inhalation to HFIB at concentrations of 6, 30, or 100 ppm for 6 hours per day for 9 exposure days. The submitter stated that analyses for induced sister chromatid exchanges (SCEs) in peripheral lymphocytes "did not indicate consistent statistically significant differences from control animals" or "a cumulative dose response." The submitter did state, however, that "there were several individual data points (4/38) that were significantly elevated above the overall mean control value" and that these differences were observed in the 10 and 100 ppm HFIB exposure groups, but not in the 30 ppm HFIB exposure group.

The submitter reported that the above studies were conducted due to the company's "renewed [but not reported] commercial interest" in hexafluoroisobutylene. In addition, the company stated that although previously conducted studies yielded "inconclusive results," the findings in the recent studies "suggest that it is reasonable to conclude that this chemical is a weak mutagen."

With regard to the previously performed studies on HFIB, the submitter reported that in an Ames Salmonella typhimurium (bacteria) assay conducted in the presence of exogenous metabolic activation and using an exposure time of 1 hour in an enclosed chamber containing a high HFIB gas concentration, the chemical caused an increase in the reversion of strain TA-1538, a slight response in TA-1537, and no response in TA-1535. The submitter also reported that when HFIB was tested in suspension, reversion frequencies were increased in TA-1538, slightly increased in TA-1537, and not increased in TA-1535. The submitting company did not state whether these particular studies were also conducted in the absence of exogenous metabolic activation.

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In another Ames assay, although HFIB reportedly induced a 2 to 3-fold "increase in histidine revertents per plate over background levels in strain TA-100 in the range of 6.4 to 22.8 percent gas in air mixture," the submitter stated that "there was no linear dose response." The submitter also stated that the observed mutagenic activity was "consistently higher" in the presence of exogenous (rat liver) metabolic activation and that there were no increases in reversion frequencies in strains TA-1538, TA-1537, TA-1535 and TA-98.

The submitting company reported that HFIB was found to be mutagenic in an in vitro L5178Y mouse lymphoma cell forward mutation assay conducted in the presence of exogenous (mouse liver) metabolic activation. The submitter did not provide any information on the levels of HFIB tested in this study and did not indicate whether the study was also conducted in the absence of exogenous metabolic activation.

The submitter reported that no effects were noted when HFIB was tested in a yeast (Saccharomyces cerevisiae (strain D4)) gene conversion mutagenicity study. The submitter did not report whether this study was conducted in the absence and/or presence of exogenous metabolic activation.

With regard to previously performed in vivo studies, the company stated that there was a slight, but not statistically significant, increase over controls in the observed frequency of structural chromosomal aberrations in the cells (unspecified) of rats exposed to 7,500 ppm HFIB for 1 hour. The submitting company stated that "there was no increase in the frequency of structural chromosomal aberrations observed in rats exposed to 5,000 ppm." In addition, the company reported that the 1-hour LC50 was found to be 7,000 ppm in this study.

The submitting company reported that the 4-hour LC50 for HFIB was found to be 1425 ppm in rats. In addition, the submitter reported that HFIB had been tested in rats via inhalation at 0, 53, or 215 ppm for 6 hours per day, 5 days per week for 2 weeks. The company stated that "all animals in the 215 ppm group either died or were killed in moribund condition after 4 exposures" and "in the 53 ppm exposure group, while all the animals survived the exposures, signs of probable respiratory tract irritation were seen, as well as an increase in kidney weight."

Finally, the submitting company stated its belief that, based on the currently available information, hexafluoroisobutylene is "moderately toxic and weakly mutagenic."

Submission Evaluation

Based on a review of the summarized experimental findings that were presented in this submission, it does appear that HFIB is, at minimum, moderately toxic in vivo and does possess some degree of in vitro/in vivo mutagenic and in vivo clastogenic activity. Further evaluation of the reported findings must await EPA's receipt of complete copies of the final reports (including data and protocols) from all of the toxicologic studies cited in the submission.

Current Production and Use

A review of the production range (includes importation volumes) statistics for hexafluoroisobutylene (CAS No. 382-10-5), which is listed in the initial TSCA Inventory, has shown that no 1977 production/importation was reported or that all of the production range data reported were claimed as Confidential Business Information by the manufacturer(s) and/or importer(s) and cannot be disclosed (Section 14(a) of TSCA; U.S.C. 2613(a)). All of the data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

No information concerning past, current, or proposed use(s) of hexafluoroisobutylene was provided by the submitting company or located in the secondary literature sources consulted.

Comments/Recommendations

The submitting company reported that an internal hexafluoroisobutylene exposure limit of 1 ppm has been established because the company has not as yet determined a no observed effect level in laboratory animals. In addition, the company reported that when hexafluoroisobutylene commercial activity is resumed, "process controls and personal protective equipment, including respirators and medical surveillance, will be utilized to limit the potential for exposure and to protect workers."

EPA's Office of Toxic Substances (OTS) has received and evaluated TSCA Section 8(e) submissions containing toxicity and/or exposure information on structural analogs of hexafluoroisobutylene (e.g., 8EHQ-1077-0011 and 8EHQ-0278-0042). The Test Rules Development Branch (TRDB/AD/OTS) is currently reviewing toxicity and exposure data on various fluoroalkenes as recommended by the Interagency Testing Committee (ITC).

a) The Chemical Hazard Identification Branch (CHIB/AD/OTS) will request the submitting company to provide complete copies of the final reports (including protocols and data) from each of the in vitro and in vivo toxicologic studies cited in its submission. In view of the Agency's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the submitting company will also be asked if it is conducting, or plans to conduct, additional studies designed to further define the toxicity of hexafluoroisobutylene and to describe the nature of such studies. In addition, the company will be informed that EPA would welcome the submission of the following types of information on hexafluoroisobutylene: 1) current and/or projected production/importation volumes, 2) past, current and/or proposed use(s), and 3) actual and/or potential consumer and environmental exposure.

b) The Chemical Hazard Identification Branch will screen the reported information in order to determine the need for further OTS assessment of hexafluoroisobutylene.

c) The Chemical Hazard Identification Branch will transmit copies of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA, ORD/EPA and TRDB/AD/EPA. A copy will also be sent to EPA's Industry Assistance Office (IAO/OTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0583-0477 S
Page 1 of 2

DATE: JUN 7 1983

SUBJECT: Status Report* 8EHQ-0583-0477 S

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Approved 6/14

Revision Needed ____________

Note

The submitting company has claimed its identity and the identity of each of the subject chemical substances as TSCA Confidential Business Information (CBI).

Submission Description

The submitting company provided summarized final results from a battery of short-term *in vitro* and *in vivo* tests on the subject chemical substances, *three of which were* reported to be intermediates. According to the submitter, all of the chemicals produced varying results in Ames *Salmonella typhimurium* (bacteria) tests. In addition, the submitter *reported that three* of the chemicals were tested in an *in vitro* Mouse Lymphoma Cell Forward Gene Mutation Assay. The *submitter* stated, however, that the positive results obtained from this *in vitro* assay were "scientifically questionable," because *guidelines* for performing the test were not rigorously followed. The submitter also reported that these three chemicals were found to be negative when tested in an *in vivo* cytogenetics assay and an "oncogenic [cell] transformation" assay. In addition, the submitter reported that due to the fact that previously obtained Unscheduled DNA Synthesis (UDS) test results were declared invalid by the performing laboratory, the tests were re-run and the three chemicals were found to give negative results.

The submitter stated that on the basis of the test data, which were received by the company in "(mostly verbal, some in draft form)," the submitter does not know "if the source of the mutagenic response derives from the compounds themselves or from impurities in the . . . raw material."

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Submission Evaluation

The submitted summarized information indicates that the tested substances may possess some degree of mutagenic activity. Complete copies of the final reports (including test protocols and data) from the cited studies should be obtained in order to properly evaluate the reported findings.

Current Production and Use

Due to the fact that the submitter has claimed the identities of the subject chemical substances as TSCA CBI, no production or use information will appear in this status report.

Comments/Recommendations

It should be noted that although a positive *in vitro* result, when considered alone, may not be sufficient to offer reasonable support for a conclusion of substantial risk, EPA does believe that *in vitro* studies do provide valuable data that can aid in assessing possible hazards/risks posed by chemicals to health and/or the environment. EPA also believes that a positive *in vitro* test result in combination with additional information (*e.g.*, knowledge of actual or potential exposure to or high production of the subject chemical substance or mixture) would, in many cases, suggest the need for further more definitive toxicologic study with the results considered for possible submission to EPA under Section 8(e) of TSCA.

In its submission, the company stated that further *in vitro* Mouse Lymphoma Cell Forward Gene Mutation Assays were being conducted with some of the subject chemicals. The company stated that EPA would be informed about the results of these additional tests.

a) The Chemical Hazard Identification Branch (CHIB/AD) will request the submitting company to provide complete copies of the final reports (including test protocols and data) from each of the *in vitro* and *in vivo* studies cited in its submission.

b) The Chemical Hazard Identification Branch will screen the reported information in order to determine if further OTS assessment of the subject chemicals is warranted.

c) The Chemical Hazard Identification Branch will provide a copy of this status report to the TSCA Assistance Office (TAO/OTS/OPTS/EPA).

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0583-0478 S
Page 1 of 3

DATE: JUN 6 1983

SUBJECT: Status Report* 8EHQ-0583-0478 S

Approved JW 6/6/83

FROM: Justine L. Welch JW Team Leader
Chemical Selection and Profiles Team/CHIB

Revision Needed

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Submission Description

The Shell Oil Company submitted a copy of a draft report of a recently completed 14-day rat skin-application study of EPON Curing Agent®D (2-ethyl hexanoic acid compounded with 2,4,6-tris[(dimethylamino)methyl]phenol; CAS No. 51365-70-9). Shell reported that signs of central nervous system (CNS) effects at doses of 0.1 ml/kg/day and above, and a dose-related incidence of mortality and time to death at doses of 1 and 5 ml/kg/day had been observed in the 14-day study. The submitter also reported that the provided preliminary information had not yet been subjected to a quality assurance review or a complete statistical analysis. With regard to the significance of the results from the 14-day rat skin-application study, the Shell Oil Company stated that:

> "The signs of CNS effects were observed at all levels tested (0.1, 1.0 and 5.0 ml/kg/day) and were seen in some animals as early as the first day of exposure. Comparable human exposure would be 5 to 7 ml/day, an unlikely but possible occupational exposure. In our consideration, this possibility and the absence thus far of a demonstrated no effect level, reasonably supports a conclusion of substantial risk. Animal mortality was observed at the two higher levels of exposure; comparable exposure in man would be 70 to 350 ml/day. The animal deaths were unexpected, particularly at the mid-range dose because of the low [previously] observed acute [rat] oral toxicity (7.1 g/kg), and contribute to our perception of substantial risk."

With regard to the toxicity observed in previously conducted studies, Shell submitted a copy of a 1951 report containing the final results of several acute in vivo toxicity studies of EPON Curing Agent®D administered via the following routes of exposure: oral (mice and rats), inhalation (rats), dermal (intact rabbit skin) , or ocular (rabbits). The results contained in the 1951 report can be summarized as follows: 1) the LD50 for mice exposed to a single oral dose was found to be in excess of 9 g/kg; 2) the ALD (approx. lethal dose) for rats exposed to a single oral dose

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***NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.**

was determined to be 7.1 g/kg; 3) the ALD for rabbits exposed via a single skin application was found to be greater than 10 g/kg; 4) repeated (4 hours daily for 9 days) inhalation exposures to saturated vapor did not produce death or any toxic symptoms in rats; 5) no signs of irritation were found following a single application of the test material to the intact skin of rabbits; and 6) progressive severe eye damage was observed in rabbits following instillation of one drop of the test material.

In its submission, the Shell Oil Company reported that it was not aware of any adverse effects having occurred as the result of using EPON Curing Agent®D. In addition, Shell stated that the existing Material Safety Data Sheet (MSDS) "recommends skin protection in the use of the product." Shell's submission also contained a copy of the existing MSDS for EPON Curing Agent®D.

Submission Evaluation

The submitted animal data indicate that EPON Curing Agent®D causes death by CNS activity at very high acute doses as evidenced by the rapidity of death (5-30 minutes) and the observed signs (clonic and epileptiform convulsions). At lower lethal doses in both the acute oral and 14-day dermal studies, CNS signs were also observed. However, the actual cause of death was probably not CNS toxicity because the time-frame is more consistent with other organ toxicity (e.g., the observed hepatotoxicity). At non-lethal doses, reversible CNS signs of lesser magnitude were observed.

Although the submitted data do not allow a complete determination of direct neurotoxic action of EPON Curing Agent®D at any dose (because no neuropathology was attempted), there is clear evidence of direct CNS activity at very high doses. Many of the CNS signs observed at the lower doses may be secondary to the other types of systemic toxicity observed.

Current Production and Use

A review of the production range (includes importation volumes) statistics for CAS No. 51365-70-9, which is listed in the TSCA Inventory, has shown that no 1977 production/importation was reported or that all of the production range data reported were claimed as confidential by the manufacturer(s) and importer(s) and cannot be disclosed (Section 14(a) of the TSCA, U.S.C. 2613 (a)). All of the data submitted for the Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

Shell reported that EPON Curing Agent®D has been used for over 30 years as an epoxy resin hardener and that the "the major uses for this curing agent are directed toward electronic and electrical encapsulation, embedment, and insulation." No additional information on the uses of the subject substance was located in the secondary literature sources consulted.

Comments/Recommendations

In the cover letter to its Section 8(e) submission, Shell stated that the reported information was being transmitted to NIOSH and OSHA, Shell employees and customers, and other companies who currently produce or have produced the product. Shell also stated that the existing EPON Curing Agent®D "Material Safety Data Sheet is being revised to reflect these new animal test data" and that a complete copy of the 14-day rat skin-application study report, upon completion, will be provided to EPA.

a) The Chemical Hazard Identification Branch (CHIB/AD/OTS) will screen the submitted information in order to determine if further OTS assessment of EPON Curing Agent®D is warranted.

b) The Chemical Hazard Identification Branch will transmit copies of this status report to NIOSH, OSHA, CPSC, NTP, FDA, OW/EPA, OSWER/EPA, OANR/EPA, and ORD/EPA. A copy of this status report will also be transmitted to the TSCA Assistance Office (TAO/OTS/EPA) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0583-0479 S
Page 1 of 6

DATE: JUN 27 1983

SUBJECT: Status Report* 8EHQ-0583-0479 S

Approved JW 6/28

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

Revision Needed ________

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Note

The submitting company has claimed its name and specific product names as TSCA Confidential Business Information (CBI). For ease in reviewing this status report, the reader's attention is directed first to the information contained in the Current Production and Use section that begins on page 4 of this report.

Submission Description

The submitting company provided the results of three acute inhalation toxicity studies involving rats exposed to vapors generated by heating/melting the chemical substances and mixture listed below. The submitter reported that these studies were conducted in response to customer concerns about possible effects of worker exposure to vapors observed during the cooling phase of plastic products manufacturing processes. The submitter also pointed out that although "no complaints or problems have been recorded in the workplace," the company "decided that an inhalation study on the vapors would be appropriate."

TEST MATERIALS

A) Polypropylene (CAS No. 9003-07-0);

B) Bis-2-hydroxyethyl-tallow amine (CAS No. 61791-44-4); or

C) Mixture (1 part A / 3 parts B)

According to the submitter, the first study involved groups of rats (10 rats/group) exposed via inhalation for 4 hours to vapors generated during the heating/melting of polypropylene (A) alone, bis-2-hydroxyethyl-tallow amine (B) alone, or C (mixture of A/B) to temperatures of 240°C, 185°C, and 235°C, respectively. With regard to the observed overall mortality, the submitter reported that 10/10, 3/10, and 9/10 rats died within the first few days following exposure to A, B, and C vapors, respectively. The submitting company stated that although these results indicated that polypropylene vapors alone or mixed with vapors of bis-2-hydroxyethyl-tallow amine were "extremely toxic to the test animals," there was great uncertainty as to whether the observed mortality was due to simple asphyxiation or due to the toxicity of certain heat decomposition products of the tested materials. The submitter also reported that due to several serious experimental deficiencies that were detected during review of the final report, it was decided that the study was not conducted by the performing laboratory in accordance with the TSCA inhalation testing guidelines and needed to be repeated.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

The submitter reported that prior to repeating the inhalation study, a quantitative analytical study (not involving animal exposure) was performed on vapors generated by heating/melting polypropylene. The company stated that in order to prevent the loss of low boiling compounds, the heating/melting process was performed without venting to the outside and further stated that this procedure was the same as that used to generate the vapors in the first acute inhalation study. The submitter reported that the analytical study showed that carbon monoxide (over 1800 ppm (detection limit)) and acetaldehyde (over 1000 ppm) were present in the polypropylene vapor. Specifically with regard to the carbon monoxide level detected in the polypropylene vapor, the submitter stated that such a level would "represent a very toxic concentration to test animals."

With regard to the repeated 4-hour inhalation study, the company stated that a revised protocol was employed that included "constant oxygen monitoring and measurement of certain polypropylene breakdown products such as carbon monoxide, carbon dioxide, propylene, and short-chain aldehydes." In addition, the submitter stated that the method used to generate the test vapors involved heating the test material in a flask that was vented to a scrubber to remove vapor and low boilers." The submitter also stated that once the test material had melted and was at the desired temperature, the container was removed from the hood and connected to the test animal exposure chamber. The heating/melting was reportedly performed this way for the following reasons: 1) the animals would not be exposed to decomposition products formed while the test materials were being initially heated/melted and brought up to the desired temperature (240°C in the case of polypropylene); and 2) this vapor "generation method more closely resembles the type [of] exposure that would occur in the workplace, where the reactors in which the polymer resins are melted are basically closed systems with vents that lead to either a scrubber or directly to the outside of the building."

With regard to the results of the repeated study, the submitter reported that although no deaths were observed for rats exposed to A or B vapors alone, 10/10 rats died over a five day period following exposure to vapors of the mixture (C). The submitter stated, however, that due to evidence that showed that the test mixture was "heated to well over 210°C with even auto-ignition occcuring at one point," the results of the second study were considered "invalid or at least inconclusive." The submitter also stated that the second study, as performed, was "not representative of the actual conditions of use" in that the submitter's workers "are not exposed to oxidized product" and customers' workers "are not exposed to [the solid product] heated more than 1 or 2 minutes."

The submitter stated that considering the experience gained from the first two studies, a third and final inhalation study was conducted under conditions that would "more closely duplicate conditions employed during actual manufacture..." The company stated that the third study, which involved a 4-hour rat inhalation exposure to vapors of the heated mixture (C) only, was conducted with the following modifications to the protocol: "(1) all heating procedures were performed under a nitrogen gas atmosphere to minimize oxidation; (2) the ethoxylated amine was heated to temperature while being stirred; (3) after the amine had reached the correct temperature, the polypropylene pellets were added to the flask, the mix was continuously stirred throughout the experiment and the mix temperature was continuously monitored and kept at 200°-210°C; (4) low boiling compounds produced during the initial heating and melting procedure were not directed into the test chamber." The submitter stated that "during the course of the inhalation study, at no time was the mix observed to be discolored, indicating that oxidation of the material was being minimized". In addition, the submitter stated that "gravimetric and particle size analysis performed during the exposure period both indicated that the chamber concentration of the test article was .4 mg/l, suggesting that very little vapor was present, but rather condensed droplets of test article."

With regard to the results of the third study, the submitting company reported that each of the 10 exposed animals exhibited salivation, nasal discharge, and labored breathing during the 4-hour exposure period. With regard to mortality, the submitter reported that although all rats survived the 4-hour exposure, 1 male rat and 1 female rat died on days 3 and 7, respectively of the 14-day post-exposure observation period. The remaining 8 animals were reported to have lost weight during the first few days and gained weight over the last few days of the 14-day post-exposure observation period. The submitting company reported that other than "some darkened areas of the lungs" of one of the exposed rats, nothing remarkable was observed during necropsy performed on all rats, including those that died on days 3 and 7.

The submitter stated that a chemical analysis that was performed during the third study "indicated that the chamber concentrations of the amine was 0.25 mg/l, which was very close to the level measured during the second inhalation study (i.e., 0.3 mg/l) and which caused the death of 100% of the test animals following a 4-hour exposure period." It was also stated that "the precautions taken during the third inhalation study to minimize oxidation significantly reduced the toxicity of the resultant atmosphere."

With regard to the results of previously performed toxicicologic studies, the submitter stated that polypropylene resin (powdered form, room temperature) is non-toxic via acute oral administration to rats (LD50 in excess of 5 g/kg), is not a primary rabbit skin irritant, and is slightly to moderately irritating to the eyes of rabbits. The submitter also noted that "it has been well documented in the literature that the heating of polypropylene in air to greater than 350°C will form lethal concentrations of toxic gases, including carbon monoxide and short-chain, highly irritating aldehydes such as acrolein and crotonaldehyde." In addition, the submitting company reported that the ethoxylated tallow amine and a 75% ethoxylated tallow amine/25% polyethylene resin mixture were shown in previous studies to be "toxic by ingestion (oral LD50 in rats is approximately 1-2 g/kg), and are severe eye and skin irritants, with probable corrosive effects." The company also submitted a copy of a paper entitled "Further Investigations into the Relative Toxicity of Decomposition Products Given Off from Smoldering Plastics" (Hofmann, H. Th. and Sand, H.; JFF/Combustion Toxicology; Vol. 1; pg. 250-8; 1974).

In conclusion, the submitting company stated that the results of the acute inhalation toxicity testing of the polypropylene/bis-2-hydroxyethyl-tallow amine mixture "show that highly irritating compounds become airborne when the test material is heated to 190°-210°C " and hypothesized that "some form of hydrocarbon is carrying [bis-2-hydroxyethyl-tallow amine], a known, severe irritant, into the lungs of the test animals." The submitter also stated that "decreasing the oxidation and degradation of the mix was shown to decrease the toxicity of the generated atmosphere."

Submission Evaluation

Based on a review of the submitted summarized results, it is apparent that, as the submitter stated, oxidation/degradation of the mixture of polypropylene and bis-2-hydroxyethyl-tallow amine renders the heat-generated vapors extremely toxic upon inhalation. It should be noted that the darkened areas of the lungs observed in one of the rats in the final acute inhalation study may have represented hemorrhage or focal congestion and may not have been the result of the heat-generated vapor of the mixture; such areas are often observed during necropsy of rats. Complete copies of the final reports from the three inhalation studies, including test protocols and data, should be obtained in order to evaluate better the reported toxicologic findings.

Current Production and Use

The submitting company stated that it currently manufactures several products grouped under a single product name (name was claimed as TSCA CBI) which are sold for use as antistatic agents in formed plastic articles (e.g., bottles and films). The submitter reported that these "antistat" products are composed of either an ethoxylated amine (e.g., ethoxylated tallow amine or ethoxylated cocoamine), or a combination of such ethoxylated amines and a plastic resin (e.g., polypropylene or polyethylene).

The submitting company stated that the mixed product is prepared by heating 1 part polypropylene and 3 parts ethoxylated tallow amine to 180-210°C (220°C maximum) for 4 hours under a carbon dioxide or nitrogen "blanket" in order to reduce oxidation and degradation. The submitter reported that during this process, a homogeneous melt is formed, cooled, and "converted to pellets that are added to the plastics to be antistat treated."

The submitter reported that in molding operations, the antistat products are mixed (in an extruder) with melted plastic resins at 200°C "to levels ranging from 0.1% to 0.3% ethoxylated amine relative to total batch size" for 1 to 2 minutes prior to the molding and cooling phases of the process. The submitter stated that the extruder is basically considered to be a closed system. The use of the antistat product in plastic film production is reported to be similar to the above described molding operation except that the final plastic product is a thin plastic sheet as opposed to a molded plastic article.

A review of the production range (includes importation volumes) statistics for polypropylene (CAS No. 9003-07-0), which is listed in the initial TSCA Inventory, has shown that between 704 million and 2.94 billion pounds were reported as produced and/or imported in 1977. A review of the production range (includes importation volumes) statistics for bis-2-hydroxyethyl-tallow amine (CAS No. 61791-44-4), which is also listed in the initial TSCA Inventory, has shown that between 11 thousand and 111 thousand pounds were reported as produced and/or imported in 1977. It should be noted that this production range information does not include any production/importation data claimed as confidential by the person(s) reporting for the initial TSCA Inventory, nor does it include any information which would compromise TSCA Confidential Business Information. The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 10).

Comments/Recommendations

In its submission, the company stated that although its current Material Safety Data Sheet (MSDS) contains a warning to "Avoid Inhalation of Vapors Generated During Processing," plant personnel and customers were being notified about the reported findings in order to re-emphasize "the need to minimize exposure to any vapors generated during manufacture and processing."

The Chemical Hazard Identification Branch (CHIB/AD/OTS) recently prepared a DRAFT Chemical Hazard Information Profile (CHIP) on acetaldehyde. The acetaldehyde monitoring information presented in this submission will be considered for inclusion in that CHIP.

a) The Chemical Hazard Identification Branch will request the submitting company to provide complete copies of the final reports (including protocols and data) from each of the acute rat inhalation studies cited in the submission.

b) The Chemical Hazard Identification Branch will screen the submitted information in order to determine if further OTS assessment of the reported findings is warranted.

c) The Chemical Hazard Identification Branch will transmit a copy of this status report to NIOSH, OSHA, CPSC, OW/EPA, OSWER/EPA, OANR/EPA, and ORD/EPA. A copy of this report will also be sent to the TSCA Assistance Office (TAO/OTS) for appropriate distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0683-0480
Page 1 of 3

DATE: JUL 6 1983

SUBJECT: Status Report* 8EHQ-0683-0480

Approved 7/12

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

Revision Needed ________

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Submission Description

Exxon Company, U.S.A. provided summarized interim results from an ongoing chronic mouse skin-painting study of a mineral seal oil product (Mentor®28). The submitter reported (by phone) that Mentor®28 is a chemically neutralized middle petroleum distillate (CAS No. 64742-30-9). According to Exxon, 25 microliters of the product have been applied 3 times per week for over two years to the skin of 50 C3H male mice. The company reported that as of May 16, 1983 (756th day of the study), only 6 Mentor®28-treated mice remained alive. Exxon stated that the study is expected to continue for another 10 to 12 weeks or until the last animal has died. Exxon Company, U.S.A. reported that as of May 16, 1983, 8/50 Mentor®28-treated mice had been observed (grossly) to have a skin tumor (a total of 3 papillomas and 5 carcinomas). In addition to the summarized interim results, the company submitted physical/chemical data, ultraviolet (UV) inspection data, and product information for Mentor®28.

Submission Evaluation

Although Exxon Company, U.S.A. did not submit any information about negative (or positive) controls, it can be inferred from the summarized information that was provided that the tested material does possess some degree of oncogenic activity toward mouse skin. According to Exxon, the final report (which should contain the study protocol(s) and data) will be completed and submitted to EPA in the latter part of 1984.

Current Production and Use

According to the TSCA Inventory, a chemically neutralized middle petroleum distillate (CAS No. 64742-30-9) is defined as a complex combination of hydrocarbons produced via a treating process to remove acidic materials. The hydrocarbons have carbon numbers predominantly in the range of C11 through C20 and boil in the range of approximately 401°F to 653°F (205°C to 345°C).

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

A review of the production range (includes importation volumes) statistics for chemically neutralized middle petroleum distillates (CAS No. 64742-30-9), which are listed in the initial TSCA Inventory, has shown that over 6.7 billion pounds were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed as confidential by those persons reporting for the TSCA Inventory, nor does it include any information that would compromise TSCA Confidential Business Information. The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

According to the provided product information, Mentor®28 can be used in a variety of industrial and household products. The industrial applications of Mentor®28 were reported to include its use as a base oil in tanning liquors for leather, as a vehicle for colored inks (e.g., heat-set inks) in newspaper printing, as a medium for chemical and vapor recovery systems, as a cordage oil for spraying and coating of light-colored twine and rope, as an instrument standardization oil, as a plasticizer for certain specialty resins, and as a replacement for diesel fuel (and other hydrocarbon streams) in oil drilling mud formulations. Household applications of Mentor®28 were reported to include the product's use as a base or diluent in disinfectants, germicides, polishes, cleaning compounds and cleaning solvents.

In addition, Exxon Company, U.S.A. reported that some of the chemically neutralized middle petroleum distillate is marketed as Somentor®43, a product which is used principally as a base oil for surface lubrication in the rolling of aluminum sheets into foil stock that may come into contact with foods.

Comments/Recommendations

Exxon Company, U.S.A. reported that all Mentor®28 and Somentor®43 customers of record and the U.S. Food and Drug Administration (FDA) are being notified about the interim chronic mouse skin-painting results.

EPA's Office of Toxic Substances (OTS) has received and evaluated many other TSCA Section 8(e) and "For Your Information" submissions that have contained toxicity/exposure information on a wide variety of petroleum process streams/products.

a) The Chemical Hazard Identification Branch (CHIB/AD/OTS) will request the Exxon Company, U.S.A. to ensure that the Agency is apprised of any new and/or significant toxicologic results from the company's ongoing chronic mouse skin-painting study of Mentor®28 and to ensure that the final report, when submitted, contains complete copies of the study protocol(s) and all data obtained. In view of EPA's general interest in company actions that are taken on a voluntary basis in response to toxicity/exposure information, Exxon Company, U.S.A. will also be requested to describe the actions it has taken to warn Exxon workers and to reduce and/or eliminate exposure to the chemically neutralized middle petroleum distillate.

b) The Chemical Hazard Identification Branch will screen the reported information in order to determine if further OTS assessment of the chemically neutralized middle petroleum distillate is warranted at the present time.

c) The Chemical Hazard Identification Branch will provide a copy of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA, ORD/EPA, and OPP/OPTS/EPA. A copy of this report will also be sent to the TSCA Assistance Office (TAO/OTS/EPA) for appropriate distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0683-0481
Page 1 of 3

DATE: JUL 15 1983

SUBJECT: Status Report* 8EHQ-0683-0481

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Approved 7/18

Revision Needed ______

Submission Description (See NOTE on Page 3 of this report)

The Phillips Petroleum Company submitted copies of Standard Operating Procedures (SOPs) and results from several in vitro genotoxicity studies of 1,2-ethanedithiol (CAS No. 26914-40-9). According to the submitter, the chemical was found to be negative in an Ames *Salmonella typhimurium* (bacteria) assay both in the presence and absence of exogenous metabolic activation. The submitter also reported that 1,2-ethanedithiol was found to be positive (without metabolic activation) and negative (with metabolic activation) in a Mouse Lymphoma Cell Forward Mutation Assay. In addition, the company reported that the chemical was found to cause an increased incidence of Sister Chromatid Exchanges (SCEs) in cultured Chinese Hamster Ovary (CHO) cells.

Submission Evaluation

Considering that Standard Operating Procedures (SOPs) do not detail actual observations or protocol changes made during the performance of toxicologic tests, the submitted SOPs are of only limited value for evaluating the reported in vitro findings. In the absence of complete copies of the final reports (including the actual study protocols and all data), it is not possible at this time to verify the accuracy of the reported results. It should be noted that the Phillips Petroleum Company submission did not contain any experimental details for the performed SCE assay in cultured Chinese Hamster Ovary (CHO) cells. The submission also contained a detailed SOP, but no experimental data, for an *Escherichia coli* (bacteria) microsuspension assay for DNA damage.

According to a provided Material Safety Data Sheet (MSDS), 1,2-ethanedithiol is a clear, combustible liquid with a pungent, nauseating odor. The MSDS indicates that over-exposure to vapors of the chemical can cause "generalized weakness, diarrhea, clonic convulsions, lacrymation, tremors, narcosis, [and] increased respiratory rate." It should be noted that 1,2-ethanedithiol is a very close structural analog to ethanethiol (ethyl mercaptan), a highly toxic chemical with a very strong, penetrating odor which is used as an odorant in natural gas.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Current Production and Use (See NOTE on Page 3 of this report)

A review of the production range (includes importation volumes) statistics for ethanedithiol (CAS No. 26914-40-9), which is listed in the initial TSCA Inventory, has shown that no 1977 production/importation was reported or that all of the production range data reported were claimed as TSCA Confidential Business Information (CBI) by the manufacturer(s) and/or importer(s) and cannot be disclosed (Section 14(a) of TSCA, U.S.C. 2613(a)). All of the data submitted for the initial TSCA Inventory, including the production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

Although the Phillips Petroleum Company did not provide any use information for 1,2-ethanedithiol, the company did state that the chemical is not marketed to the public. The submitting company also stated that exposure to the chemical is minimal because the "odor mandates that it be produced, stored, transported, and consumed in enclosed systems." No information concerning the use of 1,2-ethanedithiol was located in the secondary literature sources consulted.

Comments/Recommendations

The Phillips Petroleum Company stated that the 1,2-ethanedithiol Material Safety Data Sheet (MSDS) had been revised to reflect the reported in vitro findings and had been transmitted to all 1,2-ethanedithiol customers and to all of the submitter's facilities that handle the chemical.

It should be noted that although a positive in vitro result, when considered alone, may not be sufficient to offer reasonable support for a conclusion of substantial risk, EPA does believe that in vitro studies do provide valuable data that can aid in the assessment of possible hazards/risks posed by chemicals to health and/or the environment. EPA also believes that positive in vitro test results in combination with additional information (e.g., knowledge of potential exposure to, or high production of, the chemical substance or mixture) would, in many cases, suggest the need for further more definitive toxicologic studies with the results of such studies considered for possible submission to EPA pursuant to Section 8(e) of TSCA.

a) **The Chemical Hazard Identification Branch (CHIB/AD/OTS) will request the Phillips Petroleum Company to provide EPA with complete copies of the full final reports (including actual experimental protocols and all data) from the in vitro Ames, Mouse Lymphoma, Bacterial DNA Damage, and SCE** assays cited in its submission. In view of the Agency's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the Phillips Petroleum Company will also be asked if it is conducting, or plans to conduct, additional studies designed to further define the toxicity of 1,2-ethanedithiol.

b) The Chemical Hazard Identification Branch will screen the reported information in order to determine if further OTS assessment of 1,2-ethanedithiol is warranted.

c) The Chemical Hazard Identification Branch will transmit copies of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA, ORD/EPA, and OPP/OPTS/-EPA. A copy will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS) for appropriate distribution.

NOTE: In a supplemental submission dated November 22, 1983, the Phillips Petroleum Company stated that the CAS Registry Number for 1,2-ethanedithiol was 540-63-6 and not 26914-40-9 as had been reported by the company in its initial TSCA Section 8(e) submission. A review of the production range (includes importation volumes) statistics for 1,2-ethanedithiol (CAS No. 540-63-6), which is listed in the initial TSCA Inventory, has shown that no 1977 production/importation was reported or that all the production range data reported were claimed as Confidential Business Information (CBI) by the manufacturer(s) and/or importer(s) and cannot be disclosed (Section 14(a) of TSCA; U.S.C. 2613(a)). All of the data submitted for the initial TSCA Inventory, including the production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

In its November 22, 1983 submission, the Phillip Petroleum Company also stated that the company was going to correct the CAS Registry Number in its 1,2-ethanedithiol Material Safety Data Sheet (MSDS) and any other company information relating to this substance.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0683-0482
Page 1 of 4

DATE: JUL 20 1983

SUBJECT: Status Report* 8EHQ-0683-0482

Approved 7/21

Revision Needed ______

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Submission Description

The International Coal Refining Company (ICRC) submitted complete copies of the final reports (including experimental protocols and data) from a series of short-term in vitro genotoxicity and acute in vivo toxicity studies of several solvent-refined coal (SRC-I) products, process intermediates, and/or wastes produced by U.S. Department of Energy (DOE) pilot plants in Ft. Lewis, Washington and Wilsonville, Alabama. ICRC reported that it is under a DOE contract to develop the SRC-I technology and to design an SRC-I "demonstration" plant. The company also reported that the SRC-I technology program includes an ongoing and comprehensive toxicity testing program which includes short-term in vitro genotoxicity studies and acute, sub-chronic, and chronic in vivo studies of the SRC-I materials. The results of the short-term in vitro and acute in vivo studies that were reported in the present submission are summarized in Tables 1. and 2., respectively of this status report.

The International Coal Refining Company stated that both "ICRC and DOE are aware of the hazards that may be associated with coal-derived materials and, as a matter of routine practice, use and insist on the use of stringent precautions in their manufacture, transportation and testing." In addition, ICRC provided copies of several SRC-I Material Safety Data Sheets and SRC-I product shipping labels.

In the cover letter to its submission, ICRC stated that the results obtained from the ongoing/planned SRC-I toxicity testing studies "are expected to be useful in future process/product safety optimization work, in the design of worker health protection programs, and in the preparation of needed premanufacturing notifications (PMN's) pursuant to the provisions of Section 5(a)(1) of TSCA." ICRC also stated that both the company and DOE are committed to insure that the SRC-I process technology "is developed in an environmentally responsible manner."

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

TABLE 1. SHORT-TERM IN VITRO RESULTS

TEST MATERIAL	AMES TEST		MOUSE LYMPHOMA ASSAY	
	ACTIVATION	W/O ACTIVATION	ACTIVATION	W/O ACTIVATION
SRC Middle Distillate (CAS No. 68911-57-9)	Negative	Negative	Positive	Negative
TSL* Middle Distillate (CAS No. Unknown)	NR**	NR**	Positive	Positive
SRC Solid Fuel (CAS No. 68409-94-9) (DMSO Extract)	Positive	Negative	Positive	Positive
TSL* Solid Fuel (CAS No. Unknown) (DMSO Extract)	Positive	Negative	Positive	Positive
Ash Concentrate (CAS No. 68131-74-8) (Saline Extract)	NR**	NR**	Positive	Negative
Ash Concentrate (CAS No. 68131-74-8) (DMSO Extract)	NR**	NR**	Positive	Negative

* ICRC reported (by phone) that TSL pertains to "Two Stage Liquefaction"

** No results reported

TABLE 2. ACUTE IN VIVO RESULTS

TEST MATERIAL	ORAL LD50 (RATS)	EYE IRRITATION (RABBITS)	SKIN IRRITATION (RABBITS)	SENSITIZATION (GUINEA PIGS)
SRC Middle Distillate (CAS No. 68911-57-9)	4-5 g/kg	moderate (washed) severe (unwashed)	NR**	probable
TSL* Middle Distillate (CAS No. Unknown)	4-7 g/kg	NR**	NR**	probable
SRC Light Oil (Naphtha) (CAS No. 68476-79-9)	NR**	severe (washed) severe (unwashed)	moderate (intact) moderate (abraded)	marked
TSL* Solid Fuel (CAS No. Unknown)	NR**	NR**	NR**	positive

* ICRC reported (by phone) that TSL pertains to "Two-Stage Liquefaction"

** No results reported

Submission Evaluation

In general, the submitted short-term in vitro results show that the tested SRC-I materials possess varying degrees of mutagenic activity in bacteria and in mammalian (mouse) cells in culture. The results of the acute in vivo toxicity studies indicate that the tested SRC-I materials can be toxic (although not extremely toxic) upon oral administration, can be irritating (in some cases severely) to the eyes, can be moderately irritating to the skin, and can provoke varying degrees of skin sensitization reactions. Further evaluation of the toxic properties of these (and possibly other) SRC-I products, process intermediates, and wastes will be possible when EPA receives complete copies of the final reports (including protocols and data) from the ongoing/planned short-term in vitro genotoxicity and acute, sub-chronic, and chronic in vivo studies.

Current Production and Use

In its submission, the International Coal Refining Company stated the "current use of SRC-I materials, in addition to being carefully controlled, is limited to research and testing purposes at a limited number of research and testing facilities."

Comments/Recommendations

In the cover letter to its TSCA Section 8(e) submission, the International Coal Refining Company stated that positive results that may be obtained as the SRC-I toxicity testing program continues will be submitted to EPA to supplement the toxicologic data already provided. The submitter also stated that "in late 1983 and early 1984, ICRC expects to publish for DOE a series of reports on the short-term portions of the overall program."

EPA's Office of Toxic Substances (OTS) has received and evaluated a number of TSCA Section 8(e) and "For Your Information (FYI)" submissions containing toxicologic and/or exposure information on a variety of coal, shale, and petroleum oil products, process intermediates, and/or waste materials.

a) The Chemical Hazard Identification Branch (CHIB/AD/OTS) will screen the reported information in order to determine if further OTS assessment of the subject coal-derived materials is warranted at the present time.

b) The Chemical Hazard Identification Branch will transmit copies of this status report to NIOSH, OSHA, CPSC, NTP, DOE, OW/EPA, OSWER/EPA, OANR/EPA, ORD/EPA, CCD/OTS, and HERD/OTS. A copy of this status report will also be provided to the TSCA Assistance Office (TAO/OTS/OPTS) for appropriate distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0683-0483 S
Page 1 of 8

DATE: AUG 19 1983

SUBJECT: Status Report* 8EHQ-0683-0483 S

Approved 8/19

Revision Needed ____________

FROM: Justine D. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Note

The submitting company has claimed its name and the name of the company sponsoring the reported studies to be TSCA Confidential Business Information (CBI). Although the submitter originally claimed the actual identities of the two tested chemicals to be TSCA CBI, the company later reported non-confidentially that one of the tested chemicals was ethylene diamine tetra (methylene phosphonic acid). According to Volume II of EPA's TSCA Chemical Substances Inventory, ethylene diamine tetra (methylene phosphonic acid) has the following CAS Registry Number: 1429-50-1. For the purposes of this status report, ethylene diamine tetra (methylene phosphonic acid) will be referred to as EDTMPA. In addition, it should be noted that in two of the submitted toxicity studies (one range-finding study and one chronic study), EDTMPA was tested in combination with the second chemical, the identity of which remains confidential (TSCA CBI). For the purposes of this status report, the second chemical will be referred to as Chemical X.

Submission Description

The submitting company provided the final reports from four 1-month range-finding studies (two in rats and two in mice) and interim reports with protocols from three ongoing chronic gavage studies (two in rats and one in mice). In addition, the company submitted several memoranda that present additional information with regard to the ongoing chronic studies. The submitter stated that the subject studies were sponsored by a company that was considering the purchase of EDTMPA from the submitter for use in a new application. According to several of the submitted experimental protocols, an oral (gavage) route of exposure was selected for the performed studies because this route will approximate human exposure to the chemical(s).

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

The four 1-month range-finding studies were conducted in order to determine the appropriate dose levels to be used in the chronic studies. In the first 1-month study in rats, Sprague-Dawley rats (5 animals/sex/group) were reported to have been dosed by gavage (gastric intubation) for 28 consecutive days with EDTMPA (aqueous solution) at doses of 0 (distilled water), 15, 150, 350, or 500 mg/kg body weight. The abstract contained in the final report of this 1-month study in Sprague-Dawley rats presented the following information:

> "No deaths occurred during the course of the study, nor were there any daily observations which indicated toxicity related to administration of [EDTMPA]. There were no changes in body weights, food consumption, or mean hematological and urine parameters which indicated any test article-related toxicity. A statistically significant increase in alkaline phosphatase levels was noted in male rats dosed at a level of 500 mg/kg body weight. Alkaline phosphatase levels were also increased in female rats at the same dosage level, however, the increase was not statistically significant when compared to the control level. No test article-related gross pathological effects were observed in any animal. A subtle difference in the histological appearance of the femur was evident between control animals and those exposed to the test article at the high-dose level (500 mg/kg BW), however, the variation was not considered a definite pathological effect related to exposure to the test compound."

In the second 1-month range-finding study in rats, Charles River CD rats (5 animals/sex/group) were reported to have been dosed by gavage for 27 consecutive days with an aqueous solution of EDTMPA in combination with Chemical X. The tested EDTMPA:Chemical X dose ratios were reported to be: 0:0 (distilled water control); 15:1.2 mg/kg/day (Group T-I); 75:5.7 mg/kg/day (Group T-II); 150:11.4 mg/kg/day (Group T-III); or 350:26.6 mg/kg/day (Group T-IV). The following information was contained in the abstract of the final report of the 1-month study in Charles River CD rats:

> "Histopathology studies performed on the femur and costochondral junction revealed an osteodystrophy of the rachitic type in all rats in the T-IV group, four of five female T-III rats and three of four male T-III rats sacrificed at the termination of the study. No histopathologic lesions were detected in the femur or costochondral junctions of T-II, T-I and Vehicle Control rats. These dystrophic lesions were interpreted as related to the test article administration. Gross lesions in other organs were of the naturally occurring type and of a severity normally expected in laboratory rats of this age."
>
> [According to the Clinical Chemistry Determinations section of the final report, "no noteworthy or statistically significant differences were observed in the alkaline phosphatase data."].

With regard to the first 1-month study in mice, it was reported that EDTMPA "was administered orally via gavage to 80 $B6C3F_1$ mice (10/sex/group) at dose levels of [0 (distilled water)], 25, 75, 150 and 300 mg/kg/day." The following information was contained in the abstract of the submitted final report:

> "Alkaline phosphatase measurements at termination in control and high-dose (Group V) animals revealed a 36%-45% increase in Group V animals of both sexes as compared to their respective control groups. These data suggest a treatment-related effect on this enzyme, although insufficient data are available to make a firm conclusion.... Chostochondral osteodystrophy was observed in treated males and females from Groups III [75 mg/kg] (3/10 males; 2/9 females), IV [150 mg/kg] (6/-10 males; 4/10 females) and V [300 mg/kg] (9/10 males; 6/9 females). This finding was considered to be minimal in affected animals from Group III and minimal to moderate in those from Groups IV and V. One male from Group IV and two males and two females from Group V which showed chostochondral osteodystrophy also showed mild femoral osteodystrophy."

In the second 1-month range-finding study conducted in mice, it was reported that EDTMPA "was administered orally via gavage to 40 $B6C3F_1$ mice (10/sex/group) at dose levels of [0 (distilled water vehicle control)], 500 and 750 mg/kg/day." The following information was contained in the abstract of the final report:

> "Dose-related elevations in serum alkaline phosphatase values, considered attributable to test material administration, were seen at Week 4. Values for treated animals of both sexes were 34-41% (low dose) and 74-77% (high dose) higher than control values. Microscopic examination of bone (femur and costochondral junction) from [EDTMPA]-treated animals revealed osteodystrophy, which was attributed to test material administration and was characterized by variable increases in the thickness of the epiphysial plate, persistent cartilage in the underlying spongiosa, osteoid deposition and periosteal hyperosteosis. Femoral osteodystrophy occurred in 4 of 10 males and 3 of 7 females in the low-dose group and 8 of 10 males and 9 of 10 females in the high-dose group; [the] changes were considered minimal at the low dose and minimal to moderate at the high dose. Costochondral osteodystrophy occurred in 9 of 10 males and 8 of 8 females in the low-dose group and 9 of 9 males and 9 of 9 females in the high-dose group; [the] changes were considered to be minimal to mild at the low dose and mild to moderate at the high dose."

The charts on the following page summarize the dose levels that were selected (based on the toxicity observed in the 1-month range-finding studies) for the ongoing 24-month and 30-month gavage studies in rats and the ongoing 18-month gavage study in mice. It should be noted that EDTMPA is being administered in combination with Chemical X in the ongoing 24-month study in Charles River CD rats.

Ongoing Chronic Gavage Studies in Rats and Mice

A. 24-Month Gavage Study (Charles River CD Rats)

Group - Dose	Males	Females
0 (Distilled Water Control)	45	45
15 mg EDTMPA : 1.2 mg $\underline{X}$ /kg/day	40	40
75 mg EDTMPA : 5.7 mg $\underline{X}$ /kg/day	40	40
150 mg EDTMPA :11.4 mg $\underline{X}$ /kg/day	40	40

B. 30-Month Gavage Study (Sprague-Dawley Rats)

Group - Dose	Males	Females
0 (Distilled Water Control)	60	60
15 mg EDTMPA /kg/day	60	60
50 mg EDTMPA /kg/day	60	60
150 mg EDTMPA /kg/day	60	60

C. 18-Month Gavage Study ($B6C3F_1$ Mice)

Group - Dose	Males	Females
0 (Distilled Water Control)	85	85
15 mg EDTMPA /kg/day	85	85
75 mg EDTMPA /kg/day	85	85

The 6-month interim report from the 30-month gavage study in Sprague-Dawley rats stated that no toxicologically significant effects had been observed following 26 weeks of dosing. The 6-month interim report from the 24-month gavage study in Charles River CD rats stated that osteodystrophy had been observed microscopically in the high dose groups. However, according to memoranda dated approximately twelve months after the starting dates of the two chronic gavage studies in rats, osteogenic sarcomas were reported to have been observed in the rats in both the 24- and 30-month studies. The charts on the following page summarize the incidences of osteogenic sarcomas reportedly observed approximately one year into the ongoing chronic gavage studies in rats.

Reported Incidence of Osteogenic Sarcoma in Rats

A. 24-Month Gavage Study (Charles River CD Rats)

Group - Dose	Males	Females
0 (Distilled Water Control)	0/45	0/45
15 mg EDTMPA: 1.2 mg $\underline{X}$ /kg/day	0/40	0/40
75 mg EDTMPA: 5.7 mg $\underline{X}$ /kg/day	1/40	0/40
150 mg EDTMPA:11.4 mg $\underline{X}$ /kg/day	6/40	0/40

B. 30-Month Gavage Study (Sprague-Dawley Rats)

Group - Dose	Males	Females
0 (Distilled Water Control)	0/60	0/60
15 mg EDTMPA /kg/day	0/60	0/60
50 mg EDTMPA /kg/day	1/60	0/60
150 mg EDTMPA /kg/day (330 mg/kg*)	5/60	1/60

* The 150 mg/kg daily dose was increased to 330 mg/kg on February 14, 1983 (approximately 10 months into study)

In one of the submitted memoranda concerning the 30-month chronic gavage study, it was stated that EDTMPA was believed to be the most likely causative agent of the observed osteosarcomas.

According to the submitted 6-month interim report of the 18-month EDTMPA gavage study in mice, no osteosarcomas had been observed. In addition, the submitter provided a memorandum stating that there was no evidence of osteogenic sarcoma observed in mice by the eleventh month of the study.

Submission Evaluation

In view of the fact that EDTMPA reportedly induces osteogenic sarcomas (as discussed below) in both Sprague-Dawley and Charles River CD rats, it is of particular interest that in the 1-month range-finding study using Sprague-Dawley rats, EDTMPA at a dose of 500 mg/kg was found to bring about a statistically significant increase in the serum alkaline phosphatase levels in male rats. Alkaline phosphatase plays a key role in the deposition of phosphorus in bone metabolism. Increased alkaline phosphatase levels were also seen at the same EDTMPA dose level in female Sprague-Dawley rats, but the increase was not statistically significant. Paralleling this lesser effect on alkaline phosphatase in the females, EDTMPA (at the highest dose tested) was reported to show some (albeit very weak) tumorigenic effect toward the bone in one of the female Sprague-Dawley rats in the ongoing 30-month gavage study. The observed disturbance of bone metabolism by EDTMPA is consistent with the histopathologic observation of osteodystrophy (i.e., defective de novo bone formation) in Charles River CD and Sprague-Dawley rats of both sexes, as well as with the tissue-specific tumorigenic effect.

EDTMPA was also reported to bring about a dose-related elevation of serum alkaline phosphatase levels, as well as osteodystrophy, in mice in both 1-month range-finding studies. Although no conclusion can be made at this time relative to the tumorigenic potential of EDTMPA toward mouse bone, it should be noted that there is a consistency in both rats and mice for the observed enzymological (alkaline phosphatase) and histopathological (osteodystrophy) effects. Due to the fact that the latency period for tumorigenesis by a given chemical agent may be notably different in different species, it is possible that EDTMPA may possess tumorigenic potential toward mouse bone. However, this potential may become manifest only after a sufficiently prolonged period of administration and/or by using other inbred strains of mice. It should also be borne in mind that the actual observation periods (11-12 months) at this stage of the studies correspond to only about one-half of the life span of the two species.

The preliminary results provided thus far for the ongoing 24-month and 30-month rat studies indicate that the incidence of EDTMPA-induced osteogenic periosteal sarcomas is dose-dependent. Furthermore, the bone tumor incidence does not appear to be influenced by combination with Chemical X (in the 24-month study). This dose-dependence lends support to the reliability of the ongoing studies, although it would also be useful to know the purity of the tested materials and the chemical identity of any impurities. Considering that the reported tumor incidences resulted from actual administration periods corresponding to only about one-half of each species life-span, the possibility exists that EDTMPA may represent a significant carcinogenic hazard. However, a more complete evaluation of the carcinogenic potential of EDTMPA and the EDTMPA:Chemical X mixture must await EPA's receipt of complete copies of the final reports from each of the chronic gavage studies. It would also be of interest to know the effect (if any) of EDTMPA exposure on fetal bone development.

Current Production and Use

A review of the production range (includes importation volumes) statistics for EDTMPA (CAS No. 1429-50-1), which is listed in the initial TSCA Inventory, has shown that no 1977 production/importation was reported or that all of the production range data reported were claimed as confidential by the manufacturer(s) and/or importer(s) and cannot be disclosed (Section 14(a); TSCA; U.S.C. 2613 (a)). The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

According to the submitter, EDTMPA is manufactured by another company (identity claimed as TSCA CBI) and is marketed by the submitter in wet cake form. Although recent production/sales data were claimed as TSCA CBI, the submitter did report that "in 1983, sales are expected to be lower [than in 1982]." The submitter also reported that "of the material sold in the United States, approximately one-third is used as a stabilizer in hydrogen peroxide, one-third is used by the precious metals industry in plating applications, and one-third is used in miscellaneous applications principally in metal chelating applications."

Other than the statements contained in several of the submitted experimental protocols that the oral route would approximate human exposure, the submission did not present any information with regard to the sponsoring company's actual or proposed use of EDTMPA. According to the information obtained from a publicly available on-line computerized data base (TOXLINE), EDTMPA may have a variety of actual/potential medical and dental applications. The TOXLINE citations (which EPA obtained by using the EDTMPA CAS Registry Number) indicate that EDTMPA has been evaluated for use as an antidote in certain types of metal poisoning and as a component of oral/dental hygiene formulations.

Comments/Recommendations

The submitter stated that the two chronic rat studies were begun in March and April 1982 and are expected to end in September and April 1984, respectively, with final reports expected in June and January 1985, respectively. The submitter also reported that the chronic study in mice "was begun in May 1982 and is expected to be terminated in November 1983, with a final report anticipated in July 1984."

Although the submitter's cover letter emphasized that "there are no known adverse effects from the use of [EDTMPA] in any of its applications, or from workplace handling of the product," the company reported that "letters are being transmitted to all customers of the product, recommending that they take appropriate steps to minimize exposure to their employees" and "similar letters will be sent to other known manufacturers of the product."

a) The Chemical Hazard Identification Branch (CHIB/AD/OTS) will request both the submitting and sponsoring companies to ensure that EPA immediately receives, when available, complete copies of further interim reports and complete copies of the final reports from the ongoing rat and mouse chronic EDTMPA gavage studies. In view of EPA's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, both companies will also be asked to describe the nature of all other studies that they are now conducting/sponsoring, or plan to conduct/sponsor, that are designed to further define EDTMPA toxicity.

In addition, both companies will be informed that the Agency would appreciate receiving additional available information pertaining to actual/potential human and/or environmental exposure to EDTMPA.

b) The Chemical Hazard Identification Branch will consider the preparation of a Chemical Hazard Information Profile (CHIP) on ethylene diamine tetra (methylene phosphonic acid).

c) The Chemical Hazard Identification Branch will transmit a copy of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA, ORD/EPA, CCD/OTS and HERD/OTS. A copy of this report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0683-0484 S
Page 1 of 4

DATE: JUL 20 1983

SUBJECT: Status Report* 8EHQ-0683-0484 S

Approved 7/21

Revision Needed

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Submission Description (See NOTE on Page 4 of this status report)

The Rohm and Haas Company provided summarized final results from a sub-acute inhalation toxicity study of a polymer dust in male and female Crl:CD(SD)BR rats. Although the submitting company claimed the actual chemical identity/composition of the subject polymer to be TSCA Confidential Business Information (CBI), the company did report that the polymer has a molecular weight of approximately 1,000,000 and contains a significant amount (approximately 35%) of respirable dust particles (5 microns or less). The Rohm and Haas Company reported that "the lack of toxicological data to confirm that finely divided organic polymers are truly nuisance dusts prompted initiation" of this study.

According to the submitted summary, 5 groups of rats were exposed to polymer dust concentrations of 0, 4.9, 48, 259, or 950 mg/m^3 for 6 hours per day, 5 days per week for two weeks. On the day after the last exposure, 8 males and 8 females from each group were sacrificed while 8 males and 8 females from both the control group and the highest dose group were held for a 3-week post-exposure observation/recovery period. The submitter reported that the obtained results indicated the induction of pneumonitis in those rats exposed to the two higher concentrations. The submitter also reported that although a reversible pneumonitis would normally be expected to result from inhalation exposure to a "nuisance dust," the pneumonitis observed in the performed study was "neither progressive nor reversible within a three week recovery period." Rohm and Haas stated that "nuisance dusts, in contrast to fibrogenic dusts which cause scar tissue to be formed in the lungs when inhaled in excessive amounts, have little adverse effect on lungs and do not produce organic disease or toxic effect." The submitter also stated that the following lung observations would be expected to be made following inhalation of nuisance dusts: "1) the architecture of the air spaces remains intact; 2) collagen (scar tissue) is not formed to a significant extent; and 3) the tissue reaction is potentially reversible."

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

The following summarized information was provided with regard to the general pathologic findings from the two-week inhalation study:

> "No effects were observed in the two lowest treatment groups compared to the controls. Inhalation of 258.6 mg/m^3 produced minimal to mild multi-focal pneumonitis. Inhalation of 949.6 mg/m^3 produced slight to moderate diffuse pneumonitis. There was no evidence of foreign body giant cells or early fibrosis. What necrosis did occur was very slight. There was no damage to the architecture of the air spaces, nor was there collagen formation. There were not enough animals at 250 mg/m^3 to hold for observation for post-exposure resolution of pneumonitis. Animals exposed at 950 mg/m^3 were held for three weeks without either progression or resolution of pneumonitis observed. Despite the adverse effects observed on deep lung tissue, no effects were observed in the upper bronchial tree where non-respirable dust would be expected to deposit."

With regard to the interpretation of the obtained results, Rohm and Haas stated that the company's internal Technical Review Committee had reached the following conclusions:

> "Pneumonitis is the expected early stage reaction to high dust concentrations, that is, concentrations which exceed the normal clearance capacity of the lung. For nuisance dusts, our [the company's] toxicologist generally expects to observe initiation of the resolution of pneumonitis within a two-week exposure period. For non-nuisance dusts, resolution may take longer or it may never occur. Failure of the pneumonitis induced by the polymer product to begin resolution within three weeks is a concern. It is possible that further investigation will establish reversibility of the induced pneumonitis over a longer period of time. Acting on the evidence in hand, however, it was concluded that the polymeric product cannot be considered just a nuisance dust."

In addition to the provided summarized toxicologic results, Rohm and Haas noted that the company's "workplace exposure limit for the respirable portion of this [polymer] material had been set at 5 mg/m^3, the same limit established by the American Conference of Governmental Industrial Hygienists [ACGIH] for the respirable portion of nuisance dusts."

Submission Evaluation

Although no adverse effects were found at 50 (47.8) mg/m^3 and below, pneumonitis was observed at the two highest concentrations tested. Both the severity of reaction and extent of the lung affected were dose related, and the effects persisted for three weeks after exposure had ceased. Therefore, the Agency is inclined to agree with the submitter that the observed effects are real and that the tested material is not simply a nuisance dust. It should be noted, however, that further studies would need to be performed in order to confirm this initial impression.

Whether and how the breathing-zone concentration and particle sizes were verified were not reported in the submission. In addition, it does not appear that unreacted feedstock(s) would be present in large quantity in the polymeric material that was tested. Due to the fact that no test data were reported on the feedstock(s), however, there is a chance that unreacted feedstock(s) may accompany the polymer at some (probably low) concentration. The possibility of an unreacted substance contributing in a major or minor way to the observed or potential toxicity cannot, therefore, be ruled out at this time.

Although the submission described the observed biological effects only in general terms, it did indicate that the inhaled particles reached the deep lung and caused necrosis, but did not alter the normal architecture of the airspaces of the lung. These observations raise several questions. what cells or tissues were necrotic? How extensive was the necrosis? How was the necrosis resolved? What was the fate of the sloughed cells that were observed in the airways? what effect did the inhaled particles have on the lung clearance ability or on resident macrophages?

The submitted summary report stated that "...alveolar septal epithelial cells and macrophages... frequently had sloughed into the lumen of the airways....macrophage necrosis was not severe." This statement suggests that there was at least a noticeable amount of macrophage necrosis. This statement also suggests that the observed pneumonitis may be complicated by a weakening of the host defense mechanisms and lung clearance, and raises questions about the possible adverse effects on immune competence due to chronic exposure. Macrophage necrosis is also important because it may lead to pulmonary fibrosis following the release of lytic enzymes in the lung by the killed macrophages. Fibrosis was not, however, detected in the three weeks following inhalation exposure to the polymeric material.

It should be noted that macrophage necrosis has been observed following inhalation of other polymeric materials. For example, in TSCA Section 8(e) submission 8EHQ-0382-0438 S et seq., respirable particulates (in vivo) and a gel or suspension of polymeric particles (in vitro), were reported to be lethal to marcrophages. Therefore, it would be of interest to see the full histopathology report upon which the present Section 8(e) submission is based, and to know what effect the subject polymeric material has on macrophages in cell culture. The present submission also raises a question concerning the potential for the inhaled polymeric material to bring about progressive and ultimately profound respiratory embarrassment with impaired lung clearance, macrophage necrosis leading to fibrosis, intercurrent infections, and bronchiectasis.

Current Production and Use

Due to the fact that the Rohm and Haas Company claimed the actual chemical identity/composition of the subject polymer to be TSCA Confidential Business Information (CBI), no production or use information for the polymer will appear in this status report.

Comments/Recommendations

a) The Chemical Hazard Identification Branch (CHIB/AD/EPA) will request the Rohm and Haas Company to provide EPA with a complete copy of the final report (including protocol(s) and data) from the company's two-week inhalation study of the subject polymer dust in rats. In view of EPA's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the Chemical Hazard Identification Branch will also ask the Rohm and Haas Company if it is conducting, or plans to conduct, additional studies designed to further define the toxicity of the subject polymer. In addition, Rohm and Haas will be requested to describe the actions the company has taken to warn workers and others and to reduce and/or eliminate exposure to the polymer.

b) The Chemical Hazard Identification Branch will screen the reported information to determine if further OTS assessment of the subject polymer is warranted.

c) The Chemical Hazard Identification Branch will provide a copy of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA, ORD/EPA, CCD/OTS, and HERD/OTS. A copy will also be provided to the TSCA Assistance Office (TAO/OTS/OPTS) for appropriate distribution.

NOTE: In further correspondence with EPA regarding this submission, the Rohm and Haas Company provided the following generic name for the tested polymeric material: "Acrylic Polymer"

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0783-0485 S
Page 1 of 3

DATE: AUG 12 1983

SUBJECT: Status Report* 8EHQ-0783-0485 S

Approved 8/12

Revision Needed ____________

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Submission Description

The CIBA-GEIGY Corporation provided a copy of a cover letter from a recent CIBA-GEIGY submission on terbuthylazine (CAS No. 5915-41-3) that had been formally sent to EPA's Office of Pesticide Programs (OPP/OPTS) pursuant to Section 6(a)(2) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). The provided cover letter contained a listing of the final reports of several acute and sub-acute in vivo terbuthylazine toxicity studies that had been submitted to OPP, certain terbuthylazine production and use information, and the following summary of the toxicologic findings:

> "...the data from a 28-day repeat dermal study in rabbits showed specific effects involving lymphoreticular organs at the lowest dose tested (500 mg/kg/day) and at higher levels which reversed during a 14-day observation period. In another study, repeated oral exposure for 13 days in pregnant rabbits (pilot toxicity study prior to teratogenicity evaluation) resulted in a no observable effect level (NOEL) of 2 mg/kg/day. This NOEL is considerably lower than that previously determined in other species including rats, mice, and dogs. The significance of these findings for humans is unknown."

Submission Evaluation

The submitted terbuthylazine toxicity information is currently under review by staff of the Hazard Evaluation Division of the Office of Pesticide Programs.

Current Production and Use

A review of the production range (includes importation volumes) statistics for terbuthylazine (CAS No. 5915-41-3), which is listed in the initial TSCA Inventory, has shown that between 1 million and 10 million pounds were reported as produced and/or imported in 1977. This production range information does not include any production/importation data claimed as confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information which would compromise TSCA Confidential Business Information (CBI). The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

The following terbuthylazine production/use information was provided by CIBA-GEIGY in the submitted cover letter:

> "Only one pesticide product containing this chemical, CIBA-GEIGY Technical Terbuthylazine, is registered in the United States. No end-use products are registered in this country. CIBA-GEIGY discontinued development of terbuthylazine in the United States in the mid-1970's for economic reasons. However, prior to the company's withdrawal on November 6, 1980 of the application for end-use registration (EPA File Symbol 100-LRA), tolerances were established in corn grain, corn fodder and forage, and sorghum forage and grain (P.P. Nos. 1F1154 and 3F1409, 40 CFR 180.333)."
>
> "At [the company's] St. Gabriel, Louisiana production facility (EPA Est. 100-LA-1), CIBA-GEIGY manufactures technical terbuthylazine for export to its parent organization, CIBA-GEIGY Limited, in Switzerland. CIBA-GEIGY also makes this chemical at St. Gabriel for use as an intermediate in certain triazine herbicides manufactured at its plant in McIntosh, Alabama (EPA Est. 100-AL-1)....CIBA-GEIGY Limited has registered end-use products in foreign countries for use as a herbicide in sorghum, pome fruits, grapes, citrus and forests, and for use as an algicide in swimming pools."

No further information on the use(s) of terbuthylazine was located in the secondary literature sources consulted.

Comments/Recommendations

It is EPA's initial determination that the reported information on terbuthylazine, once formally submitted to the Agency pursuant to Section 6(a)(2) of FIFRA, need not have been also reported to the Agency under TSCA Section 8(e). According to Part VII(b) of EPA's March 16, 1978, TSCA Section 8(e) policy statement ("Statement of Interpretation and Enforcement Policy; Notification of Substantial Risk" 43 FR 11110), information need not be reported under Section 8(e) if the information "has been submitted in writing to EPA pursuant to mandatory reporting requirements under TSCA or any other authority administered by EPA (including the Federal Insecticide, Fungicide and Rodenticide Act...)."

In its submission, CIBA-GEIGY stated that the company is informing its plant personnel about the reported toxicologic findings. In addition, CIBA-GEIGY stated that the company plans to "re-evaluate its personnel protection procedures to ensure that the work force is adequately protected from over-exposure to terbuthylazine." The submitter also stated that "additional rabbit studies [on terbuthylazine] have been initiated and are expected to be available in late 1983."

a) In view of EPA's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the Chemical Hazard Identification Branch (CHIB/AD/OTS) will request the CIBA-GEIGY Corporation to describe the actions it has taken to notify non-CIBA-GEIGY personnel about the reported toxicologic findings on terbuthylazine. The submitter will also be requested to describe the actions the company has taken or plans to take to reduce and/or eliminate exposure to terbuthylazine.

b) The Chemical Hazard Identification Branch will transmit a copy of this status report to the Office of Pesticides Programs. Copies of this status report will also be provided to NIOSH, OSHA, CPSC, FDA, OW/EPA, OSWER/EPA, OANR/EPA, ORD/EPA and to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for appropriate distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: AUG 16 1983

SUBJECT: Status Report* 8EHQ-0783-0486

Approved 8/18

Revision Needed ______

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Submission Description

The Allied Corporation submitted summarized results of two acute rabbit dermal toxicity studies of hydroxylamine sulfate (CAS No. 10039-54-0). In the first study, hydroxylamine sulfate was reportedly applied as a solution under a gauze patch to the skin of New Zealand white rabbits (5 males and 5 females/group) at doses of 2.0, 1.5, 1.0, or 0.5 g/kg. Allied reported that the length of exposure was 24 hours and that the post-exposure observation period was 14 days. The following summarized information was presented by the company with regard to the results obtained from the first acute dermal exposure study:

> "The LD50 of the material in this test was found to be between 1.5 and 2.0 g/kg. Absorption through the skin was confirmed as seen by the following effects: cyanosis and hypothermia for the first several days post exposure. Reductions in red blood cell counts, increases in reticulocyte counts and enlarged spleens were observed at sacrifice 14 days post exposure. These effects suggest that the hematopoietic system is the primary systemic target organ. It was also noted that these effects may have extended down to the lowest dose level tested (0.5 g/kg), but the results at this level are not clearly defined."

The Allied Corporation reported that another acute rabbit dermal toxicity study was conducted in order to determine whether the adverse effects observed in the first study would occur at lower dose levels of hydroxylamine sulfate. The following information was presented by the company with regard to the second study:

> "The rabbits were divided into four groups consisting of two animals each. Hydroxylamine sulfate, moistened with an equivalent weight of distilled water, was applied to the shaved backs of the test animals at dose levels of 0.1, 0.05, and 0.01 g/kg. The two control rabbits were treated with distilled water alone (0.1 g/kg). Because of the small quantities

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

of hydroxylamine sulfate, the test material was held in place with an inverted plastic cover rather than gauze to prevent loss of material in the mesh of the gauze. Exposure was for 24 hours. Four days after dosing, blood was collected from the marginal ear vein for hematological analyses. The results of this study indicate that hydroxylamine sulfate induced a hemolytic anemia in a dose responsive manner. A severe hemolytic crisis was apparent in the two animals dosed at 0.1 g/kg. One of these animals died during the bleeding procedure. A no-effect level was not established in this probe [study] since a slight hematological effect may have been present at the lowest dose level (0.01 g/kg)."

Allied stated that the results of the performed studies "indicate that dermal absorption of hydroxylamine sulfate in rabbits may occur at low exposure levels and that this absorption can lead to blood dyscrasia." In addition, the submitter stated that "these blood effects are well documented in the published literature, but they may result from different routes of exposure."

The Allied Corporation also reported that hydroxylamine sulfate is a "potential sensitizer upon dermal exposure." With regard to the potential for sensitization, Allied stated that the company "recommends minimum contact either by dermal or inhalation exposure routes." Allied stated that the precautions taken to avoid sensitization "will be more than sufficient to also avoid hemolytic effects from potential dermal absorption and, therefore, Allied believes that there should not be a substantial risk of hemolytic effects from proper use of this material."

Submission Evaluation

The unique information contained in this notice is reported to be the route (dermal) of hydroxylamine sulfate exposure and the low dosage (down to 10 mg/kg) that caused dose-related reproducible adverse hematologic effects in rabbits. In addition, the rabbit dermal LD50 that was reported is an improvement over the minimal information contained in the published (1980) NIOSH Registry of Toxic Effects of Chemical Substances (RTECS) for this chemical. The spectrum of the adverse effects noted in the acute rabbit dermal toxicity studies is indeed interesting, even though some or all of the effects have been observed at higher doses in other species.

Due to the fact that hydroxylamine sulfate can decompose to hydroxylamine and sulfuric acid, the effects of hydroxylamine itself need to be considered. Both hydroxylamine and sulfuric acid can be corrosive to mucous membranes and skin. Dermal corrosion would facilitate the uptake of hydroxylamine (and its sulfate) through the skin, allowing greater systemic toxicity. Hydroxylamine has been reported in the scientific literature to cause hematuria (possibly the result of red blood cell (RBC) lysis and/or renal damage), proteinuria (possibly the result of renal damage), and methemoglobinemia. It has also been reported that hydroxylamine possesses some degree of clastogenic (and mutagenic) activity. The possibility exists, therefore, that there may be an adverse effect on hematopoiesis. It should also be noted that reticulocyte formation and an enlarged spleen both may be caused by hemolysis and hemolysis may be a function of direct RBC lysis or methemoglobin formation.

The observed hemolytic effects were reported to be severe in those rabbits exposed dermally to hydroxylamine sulfate for 24 hours at a dose of 0.1 g/kg, and there were "slight" but otherwise undefined hematologic effects observed at the 0.01 g/kg (10 mg/kg) dose level. Due to the fact that the latter dose was the lowest dose tested in the two experiments, a no-observed-effect level (NOEL) could not be determined.

One of the more interesting adverse health effects reported in this submission may be the potential for hydroxylamine sulfate to cause sensitization. Although no test data were presented for sensitization, it is possible that if both hemolysis and sensitization were part of a single pathologic entity, such as the human disease, acquired hemolytic anemia, it might yield a model for the study of such diseases.

It should also be noted that the Allied Corporation provided a copy of the company's hydroxylamine sulfate Product Safety Data Sheet in which it was reported that the chemical had been found to possess in vitro mutagenic activity, had been shown not to be carcinogenic in long-term animal studies (animal species and dose not specified), and had been shown in one in vitro study to possess spermicidal effects. It would be of interst to know the literature (or other source) citations for these findings.

Current Production and Use

A review of the production range (includes importation volumes) statistics for hydroxylamine sulfate (CAS No. 10039-54-0), which is listed in the initial TSCA Inventory, has shown that between 110 million and 551 million pounds of this chemical were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed as confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information which would compromise TSCA Confidential Business Information. The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

Secondary literature sources indicate that hydroxylamine sulfate is used as a reducing agent, as a dehairing agent for hides, as a purification agent for aldehydes and ketones, in making oximes for paints and varnishes, in rustproofing operations, as a nondiscoloring short-stopper for synthetic rubbers, as an oxidation inhibitor for fatty acids and as a photographic developer.

Comments/Recommendations

The submitted Product Safety Data Sheet recommends the use of safety glasses, impervious gloves and disposable work cloths when working or coming in contact with hydroxylamine sulfate. With regard to respiratory protection, the Product Safety Data Sheet recommends that a "full-face high efficiency particulate respirator" be used if dusty conditions exist.

a) The Chemical Hazard Identification Branch (CHIB/AD/OTS) will request the Allied Corporation to submit complete copies of the final reports (including actual test protocols and data) from the two acute dermal toxicity studies that were cited in the submission. In addition, Allied will be requested to provide literature (or other source) citations for the summarized toxicity findings presented in the Chronic Toxicity section of Allied's Product Safety Data Sheet on hydroxylamine sulfate.

b) The Chemical Hazard Identification Branch will screen the submitted information in order to determine if further OTS assessment of hydroxylamine sulfate is warranted.

c) The Chemical Hazard Identification Branch will transmit copies of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA and ORD/EPA. A copy of this report will also be transmitted to the Industry Assistance Office (IAO/OTS/OPTS).

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0783-0487 S
Page 1 of 3

DATE: AUG 24 1983

SUBJECT: Status Report* 8EHQ-0783-0487 S

Approved 8/24

Revision Needed

FROM: Justine L. Welch, Team Leader JW
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Submission Description

The American Cyanamid Company submitted a one-page letter that stated that the results of a Draize test had shown that a derivative of nicotinic acid was corrosive to rabbit eyes. The exact identity of the tested chemical was claimed by the submitter to be TSCA Confidential Business Information (CBI).

Submission Evaluation

Due to the fact that the submission did not contain any data from the performed Draize test, an evaluation of the reported rabbit eye toxicity is not possible at this time. According to the submitting company, a full report of the subject study will be sent to EPA in the near future.

Current Production and Use

Although the exact identity of the nicotinic acid derivative was claimed to be TSCA CBI, American Cyanamid did report that the "status of this compound is that of a research chemical." The submitter did not provide any information concerning the actual or proposed use(s) of the chemical nor was any use information located in the secondary literature sources consulted.

Comments/Recommendations

It should be noted that it has been EPA's longstanding policy that certain types of acute toxicity information may not warrant submission to EPA pursuant to Section 8(e), the substantial risk information reporting provision of the Toxic Substances Control Act (TSCA). The basis for the Agency's position is as follows:

> The preface to Part V of EPA's March 16, 1978, TSCA Section 8(e) policy statement ("Statement of Interpretation and Enforcement Policy; Notification of Substantial Risk" 43 FR 11110) states that "a substantial risk of injury to health or

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the environment is a risk of considerable concern because of (a) the seriousness of the effect...and (b) the fact or probability of its occurrence." With regard to the seriousness of the effect, Part V explains that the Agency considers the health effects for which "substantial risk" information must be reported to include "any pattern of effects or evidence which reasonably supports the conclusion that the chemical substance or mixture can produce cancer, mutation, birth defects, or toxic effects resulting in death, or serious or prolonged incapacitation." Information with respect to these effects can be obtained directly or inferred from designed studies (e.g., in vivo experiments and tests as described in Part VI of the 8(e) policy statement). With regard to the "fact or probability of its occurrence" criterion, Part V also explains that certain types of health effects are so serious that relatively little weight should be given to a chemical's exposure in determining whether a risk is substantial.

EPA's response to Comment 14 in Appendix B of the March 16, 1978, Section 8(e) policy statement provides additional guidance with regard to the Section 8(e)-reportability of results obtained from routine acute in vivo range finding tests (e.g., LD50 determinations, skin/eye irritation tests, etc). In its response, the Agency stated that "many routine tests are based on knowledge of toxicity associated with a chemical..." EPA's response also directed that unknown effects which occur and are observed and/or determined during acute in vivo range-finding tests may have to be reported if such effects are serious and meet the reporting requirements set forth in Parts V and VI of the policy statement.

Thus, when evaluating the results of acute animal toxicity studies for submission pursuant to TSCA Section 8(e), the Agency believes that submitting companies should consider such factors as the lethal dose, pH, route of administration, the occurrence of unexpected effects (which could be obtained via "cage-side" observations, during necropsy, etc.), and the extent and pattern of the actual/potential exposure to the tested chemical substance(s). In general, when evaluating such information for Section 8(e) reporting, the greater the acute toxicity, the less heavily a company should weigh exposure to the subject chemical(s), and vice versa.

In light of the preceeding discussion, it would appear that the results of the acute rabbit eye irritation study of the nicotinic acid derivative (as presented by the American Cyanamid Company) are not of the type warranted for submission to EPA pursuant to Section 8(e) of TSCA. In making this statement, however, it must be understood that EPA may not be aware of additional pertinent information that may have been available to and/or considered by the American Cyanamid Company in reporting the subject information to EPA under TSCA Section 8(e).

a) The Chemical Hazard Identification Branch (CHIB/AD/OTS) will request the American Cyanamid Company to ensure that the Agency receives a complete copy of the final report (including test protocol(s) and data) of the acute rabbit eye irritation study of the nicotinic acid derivative. In addition, American Cyanamid will be asked to provide the company's rationale as to why the acute eye toxicity findings warranted submission to EPA pursuant to Section 8(e) of TSCA. In view of the Agency's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the submitting company will also be requested to describe the actions it has taken to warn workers and others and to reduce or eliminate exposure to the subject chemical.

b) The Chemical Hazard Identification Branch will transmit copies of this status report to NIOSH, OSHA, CPSC, FDA, OW/EPA, OSWER/EPA, OANR/EPA and ORD/EPA. A copy of this status report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0783-0488
Page 1 of 3

DATE: AUG 26 1983

SUBJECT: Status Report* 8EHQ-0783-0488

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Approved 8/26

Revision Needed ____________

Submission Description

The Dow Chemical Company provided interim results from a chronic toxicity/oncogenicity study of acrylamide (CAS No. 79-06-1) that is being sponsored by the Dow Chemical Company, the American Cyanamid Company, the Nalco Chemical Company, and the Standard Oil Company (Ohio). This 2-year study (which is being conducted at the Dow Toxicology Research Laboratory) involves groups of Fischer 344 rats (90 rats/sex/group) exposed via the drinking-water to acrylamide at dose levels of 0, 0.01, 0.1, 0.5, or 2.0 mg/kg/day. Sacrifices of 10 rats/sex/group were performed at 6, 12, and 18 months with 60 rats/sex/group scheduled for sacrifice at termination of the study.

In its submission, Dow provided the following summarized information with regard to the histopathologic results for female rats exposed to acrylamide at the 2.0 mg/kg/day dose level:

1) "Neoplasms were statistically significantly increased in female rats at the 2.0 mg/kg/day dose level for the following organs: central nervous system (brain and spinal cord), mammary gland, clitoral gland, uterus, oral cavity, pituitary gland, thyroid gland.

2) The degree of tibial nerve degeneration was statistically significantly increased in female rats at the 2.0 mg/kg/day dose level. (Anticipated result per previously published report: Burek, J.D.; Albee, R.R.; Beyer, J.E.; Bell, T.J.; Carreon, R.M.; Morden, D.C.; Wade, C.E.; Hermann, E.A.; Gorzinski, S.J.; 1980 "Subchronic Toxicity of Acrylamide Administered to Rats in the Drinking Water Followed by Up to 144 Days of Recovery," Journal of Environmental Pathology and Toxicology, 4:157-182)."

Dow also reported that an analysis of the male rat mortality data showed a statistically significant increase in mortality at the 2.0 mg/kg/day dose level.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

It should be noted that Dow previously reported ("For Your Information" submission number FYI-OTS-1282-0223) that there was "increased mortality for female rats at the 2.0 mg/kg/day dose level of acrylamide and an increased number of female rats with a grossly observed mass in the mammary region (suggestive of a mammary tumor) at the 2.0 mg/kg/day dose level of acrylamide."

In the cover letter to its Section 8(e) submission, Dow reported that "upon completion of the remaining portions of this study including light microscopic examination of the tissues from male rats and the electron microscopic examination of the tibial nerves from male rats, final conclusions will be reported and submitted to the Agency."

Submission Evalulation

The interim chronic toxicity/oncogenicity findings for acrylamide that were reported in this submission are currently under review by both the Test Rules Development Branch (TRDB/AD/OTS) and the "Existing Chemicals Task Force" (ECTF/OTS).

Current Production and Use

A review of the production range (includes importation volumes) statistics for acrylamide (CAS No. 79-06-1), which is listed in the initial TSCA Inventory, has shown that between 10 million and 51 million pounds were reported as produced and/or imported in 1977. This production range information does not include any production/importation data that were claimed as confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information which would compromise TSCA Confidential Business Information. The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

The major applications of acrylamide include the chemical's use as a cross-linking agent, in certain adhesive formulations, in paper and textile sizes, as a soil conditioning agent, as a flocculant, and in sewage and waste treatment.

Comments/Recommendations

In its submission, the Dow Chemical Company reported that in accordance with longstanding corporate policy, Dow is immediately notifying its employees, its acrylamide customers, and other acrylamide producers. The Dow Chemical Company also reported that it is "recommending that work situtations where acrylamide is encountered be reviewed to make sure the current ACGIH TLV of 0.3 mg/cubic meter - skin (0.6 mg/cubic meter short-term exposure limit) is not being exceeded."

In 1976, NIOSH (National Institute for Occupational Safety and Health) published a "Criteria Document" relating to occupational exposure to acrylamide. In April 1978, acrylamide was designated by the Interagency Testing Committee (ITC) for certain types of health and environmental effects testing pursuant to Section 4 of TSCA. In addition, TSCA Section 8(a) and 8(d) chemical information reporting rules for acrylamide have been published by EPA. EPA has also received and reviewed several "For Your Information (FYI)" submissions containing toxicity and/or exposure data on acrylamide.

a) The Chemical Hazard Identification Branch (CHIB/AD/OTS) will request the Dow Chemical Company to ensure that EPA receives complete copies of all future interim reports and a complete copy of the final report (including actual study protocol(s) and data) from the 2-year drinking-water study of acrylamide in rats.

b) The Chemical Hazard Identification Branch will transmit copies of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA, ORD/EPA, TRDB/AD/OTS, and to the OTS "Existing Chemicals Task Force (ECTF)." A copy will also be provided to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution. (Copies of the submission itself were provided (by CHIB) to TRDB and ECTF immediately upon CHIB's receipt of the information.)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: AUG 26 1983

SUBJECT: Status Report* 8EHQ-0883-0489

Approved 8/26

Revision Needed ______

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Submission Description

Lonza, Inc. submitted summarized final results from a series of Ames *Salmonella typhimurium* (bacteria) mutagenicity assays with diethyl toluene diamine (CAS No. 68479-98-1). According to the submitter, the results of these short-term *in vitro* tests (which were conducted both with and without exogenous metabolic activation) show that diethyl toluene diamine causes a dose-dependent mutagenic response in the presence of metabolic activation.

Submission Evaluation

Although the submitted information does indicate that diethyl toluene diamine possesses some degree of mutagenic activity in bacteria, complete copies of the final reports (including the actual test protocols and data) should be requested in order to evaluate the reported *in vitro* findings more properly.

Current Production and Use

A review of the production range (includes importation volumes) statistics for diethyl toluene diamine (CAS No. 68479-98-1), as listed in the initial TSCA Inventory, has shown that no 1977 production/importation was reported or that all of the production range data reported were claimed as confidential by the manufacturer(s) and/or importer(s) and cannot be disclosed (TSCA Section 14(a), U.S.C. 2613 (a)). All of the data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

According to the information contained in a recent American Chemical Society publication (CHEMCYLOPEDIA; 1982-1983), diethyl toluene diamine has the following applications: as an extender and curing agent for polyurethane, as a curing agent for epoxy resins, and as a chemical intermediate.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Comments/Recommendations

Although a positive in vitro genotoxicity test result, when considered alone, may not be sufficient to offer reasonable support for a conclusion of substantial risk, EPA does believe that in vitro studies do provide valuable data that can aid in assessing possible hazards/risks posed by chemicals to health and/or the environment. The Agency also believes that positive in vitro test results, in combination with additional information (e.g., knowledge of potential exposure to, or high production of, the chemical substance or mixture), would suggest, in many cases, the need for further more definitive toxicologic study with the results of such studies considered for possible submission to EPA pursuant to Section 8(e) of TSCA.

a) The Chemical Hazard Identification Branch (CHIB/AD/OTS) will request Lonza, Inc. to provide complete copies of the final reports (including actual test protocols and data) from the Ames assays cited in the submission. In view of EPA's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, Lonza, Inc. will be asked to describe those actions the company has taken to warn workers and others and to reduce or eliminate exposure to diethyl toluene diamine. Lonza, Inc. will also be asked to describe the studies that the company is now conducting/sponsoring, or plans to conduct/sponsor, that are designed to further define the toxicity of diethyl toluene diamine.

b) The Chemical Hazard Identification Branch will screen the submitted information in order to determine if further OTS assessment of diethyl toluene diamine is warranted at the present time.

c) The Chemical Hazard Identification Branch will transmit a copy of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA, ORD/EPA and TRDB/AD/OTS. A copy of this status report will also be transmitted to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0883-0490
Page 1 of 4

DATE: SEP 14 1983

Approved 9/19

SUBJECT: Status Report* 8EHQ-0883-0490

Revision
Needed ________

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Submission Description

The CIBA-GEIGY Corporation submitted complete copies of the final reports from several short-term in vitro and in vivo genotoxicity studies of Araldite PT-810 (1,3,5-tris(oxiranylmethyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione; CAS No. 2451-62-9). According to the submitter, positive results were obtained in an in vitro Ames Salmonella typhimurium (bacteria) assay and in in vivo nucleus anomaly and Sister Chromatid Exchange (SCE) assays of the bone marrow cells of Chinese hamsters treated orally with Araldite PT-810. The CIBA-GEIGY Corporation also reported that the results of two other short-term in vitro assays (a Balb-c/3T3 mouse cell transformation assay and an Escherichia coli (bacteria) WP2 uvrA point mutation assay) were negative. With regard to the positive in vivo genotoxicity results, the submitter reported that the "relative concentrations and [oral] route employed are totally irrelevant to human exposure."

In addition to the provided genotoxicity information, CIBA-GEIGY submitted an Araldite PT-810 Material Safety Data Sheet (MSDS) that states that the chemical is toxic via oral and dermal exposure and may cause eye, skin, and respiratory tract irritation; dermatitis; nosebleeds; and loss of appetite. The submitted MSDS also provides the following summarized acute animal toxicity information for Araldite PT-810:

LD50 (oral):	400 mg/kg	(rats)
LD50 (dermal):	>3 g/kg	(rats)
Irritation (dermal):	Mild	(rabbits)
Irritation (eye):	Severe	(rabbits)
Sensitization (dermal):	Mild	(guinea pigs)

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Submission Evaluation

The submitted data show that Araldite PT-810 is mutagenic in *Salmonella typhimurium* (bacteria) strains TA 98, TA 100, and TA 1535 when tested with and without exogenous metabolic activation. The chemical did not produce a mutagenic response in *Escherichia coli* WP2 uvrA (bacteria) when tested under the same conditions. *S. typhimurium* strain TA 98 detects frameshift mutagens; strain TA 100 detects both base-pair and frameshift mutagens; strain TA 1535 and *E. coli* WP2 uvrA detect base-pair mutagens. Araldite PT-810 was most active when tested with *S. typhimurium* stain TA 98 (the peak activity with this strain was 8.3 times the number of mutant colonies seen in control cultures). The peak activity with *S. typhimurium* strains TA 100 and TA 1535 was 3.8 and 3.6 times background, respectively. These findings indicate that Araldite PT-810 is primarily a frameshift mutagen. Due to the fact that *S. typhimurium* strains TA 100 and TA 1535 detect mutation at the same site in the genome, it is reasonable that the tested chemical is equally active in these strains. Although *E. coli* and *S. typhimurium* are closely related Gram negative bacteria, there are sufficient differences in their genomes that differences in mutagenic activity observed following exposure to the same chemical agent are not unexpected. For example, a chemical that affects histidine biosynthesis in *S. typhimurium* need not necessarily be expected to affect tryptophan synthesis in *E. coli*. Therefore, the negative response observed in *E. coli* does not lessen the significance of the positive mutagenic response observed in *S. typhimurium*.

The submitted data also show that Araldite PT-810 can induce both Sister Chromatid Exchanges (SCEs) and nuclear anomalies in the femoral bone marrow of Chinese hamsters following oral administration of the chemical at doses of 140, 280, or 560 mg/kg in the SCE assay and 280, 560, or 1120 mg/kg in the assay for nuclear anomalies. These results demonstrate that Araldite PT-810 is capable of inducing chromosomal alterations *in vivo*.

Although Araldite PT-810 was not found to induce morphological transformation in cultured Balb-c/3T3 (mouse) cells when tested without metabolic activation, the results of the Ames *Salmonella typhimurium* (bacteria) assay show that the chemical is a direct-acting mutagen (i.e., does not require metabolic activation in order to exert a mutagenic effect). Therefore, there is no reason to believe that the addition of metabolic activation in the *in vitro* Balb-c/3T3 cell transformation assay would have significantly affected the observed negative results. It should also be noted that while the correlation between positive results obtained in *in vitro* cellular transformation assays and *in vivo* carcinogenicity studies are generally well correlated, there is a false negative rate which in the Balb-c/3T3 system can approach 50% (Heidelberger *et al.*, *Mutation Research* 114:283-385; 1983). Due to the fact that the number of known noncarcinogens tested in the Balb-c/3T3 cell transformation assay is limited, nothing can be said about the ability of this *in vitro* assay to accurately identify noncarcinogens. The observed negative response in the cultured Balb-c/3T3 mouse cell transformation assay, therefore, does not outweigh the positive responses observed in the Ames Salmonella typhimurium assay and the in vivo SCE and nuclear anomaly assays.

Current Production and Use

A review of the production range (includes importation volumes) statistics for Araldite PT-810 (CAS No. 2451-62-9), which is listed in the initial TSCA Inventory, has shown that between 20 thousand and 200 thousand pounds of this chemical were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed to be confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information which would compromise TSCA Confidential Business Information. The data submitted for the TSCA Inventory, including the production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

The CIBA-GEIGY Corporation reported that Araldite PT-810 is a trifunctional solid epoxy resin which is used only in industrial applications. The following industrial applications were listed in a submitted Araldite PT-810 Product Information Sheet: powder coatings, casting/potting, molding compounds, structural laminates, and adhesives. CIBA-GEIGY stated that in these industrial aplications, Araldite PT-810 "becomes a highly crosslinked, high molecular weight, insoluble and inert material."

Comments/Recommendations

In the cover letter to its submission, the CIBA-GEIGY Corporation reported that the company "plans to review its MSDS, label, and technical product bulletin with a view to supplying current safety information." In addition, CIBA-GEIGY reported that customer notification letters were being considered.

Although a positive genotoxicity test result, when considered alone, may not be sufficient to offer reasonable support for a conclusion of substantial risk, the Agency believes that such results are of value in assessing possible risks posed by chemicals to health and/or the environment. EPA also believes that positive genotoxicity test results in combination with additional information (e.g., knowledge of potential exposure to, or high production of, the chemical substance or mixture), would suggest, in many cases, the need to conduct additional toxicologic studies with the results of such testing considered for possible submission to EPA pursuant to Section 8(e) of TSCA.

a) In light of EPA's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, CIBA-GEIGY will be asked to describe the studies that the company is now conducting/sponsoring, or plans to conduct/sponsor, that are designed to further define Araldite PT-810 toxicity.

b) The Chemical Hazard Identification Branch will screen the submitted information in order to determine if further OTS assessment of Araldite PT-810 is warranted at the present time.

c) The Chemical Hazard Identification Branch will transmit copies of this status report to NIOSH, OHSA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA, ORD/EPA, and the Test Rules Development Branch (TRDB/AD/OTS). A copy of this status report will be sent to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0983-0491 S
Page 1 of 2

DATE: OCT -5 1983

SUBJECT: Status Report* 8EHQ-0983-0491 S

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Approved 10/11

Revision Needed ________

Submission Description

The U.S. members of the International Chlorinated Paraffin Producers Testing Consortium submitted the results from acute and chronic toxicity studies of chlorinated paraffin in *Daphnia magna* and *Chironomous tentans* (midge). In the cover letter, it was stated that these two studies, as well as assessments of the ready and inherent biodegradability of chlorinated paraffin and chlorinated paraffin toxicity studies in mussels (60-day study), rainbow trout (60-day study), and marine alga, had been conducted in accordance with a "Negotiated Testing Agreement" under Section 4 of TSCA. The cover letter also stated that the decision to submit the results under Section 8(e) was "not based upon any individual study but results from cummulative assessment of data received to date." With the submission of the reports of the *Daphnia magna* and *Chironomous tentans* studies, the Agency has now received copies of the results from each of the above referenced studies/assessments. According to the submitter, the adverse biologic activity observed in the performed studies "was limited to a short chain length highly clorinated paraffin." It was also reported that non-biodegradability was found and that bioconcentration had been observed in trout and mussels. The submitter stated that an "assessment of [chlorinated paraffin] levels present in the environment is a key to interpreting the meaning of these data."

Submission Evaluation

Although the finding of serious toxicity to aquatic species due to exposure to low concentrations of a chemical substance is in and of itself of considerable concern, the level of concern is raised significantly when such toxicity is caused by a chemical that bioaccummulates and/or is not readily biodegradable. All of the cited chlorinated paraffin studies/assessments are under review by staff of the Test Rules Development Branch (TRDB/AD/OTS) and "Existing Chemicals Task Force" (ECTF/AD/OTS) in conjunction with staff of the Environmental Effects Branch (EEB/HERD/OTS).

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Current Production and Use

The chlorinated paraffins are a family of chlorinated compounds that are derived from primarily saturated, straight-chain hydrocarbons. The maximum amount of chlorination that is achievable is 70% by weight. In general, the chloroparaffins are viscous liquids, with viscosity increasing as the percent chlorine increases. These compounds are considered to be soluble in oils and oil solvents, insoluble in water, readily emulsifiable, and nonflammable. Chlorinated paraffins are used as fire retardants, as placticizers and as additives in extreme pressure lubricants. It should be noted that chlorinated paraffins are used in some applications as substitutes for polychlorinated biphenyls (PCBs), a class of chemical substances that are strictly regulated.

Comments/Recommendations

The U.S. members of the International Chlorinated Paraffin Producers Testing Consortium reported that they are planning to conduct a field study "to determine the levels of chlorinated paraffin present in various aqueous environments." It was also reported that this study will be started as soon as possible and that the results will be submitted to EPA.

a) The Chemical Hazard Identification Branch (CHIB/AD/OTS) will send a copy of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA, ORD/EPA, TRDB/AD and the "Existing Chemicals Task Force." A copy will also be transmitted to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: OCT 20 1983

SUBJECT: Status Report 8EHQ-0983-0492 S

Approved 10/20

Revision Needed ______

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CHIB

TO: Frank D. Kover, Chief
Chemical Hazard Identification Branch/AD

Submission Description

Although the submitting company claimed its name and the exact identity of the subject chemical to be TSCA Confidential Business Information (CBI), the company did report nonconfidentially that the subject chemical was an aliphatic carbamate. According to the submission, an acute rat inhalation study was conducted with the residue obtained from an aerosol of aliphatic carbamate. The following summarized information was submitted by the company with regard to this study:

> "The aerosol was aspirated with sufficient air to vaporize substantially all of the water. The remaining material was classified by particle size and a stream containing 99% respirable solid particles having an aerodynamic mass mean diameter of 1-2 [microns] was separated for the test. These particles were introduced into an exposure chamber containing six rats. At an airborne concentration of about 0.06 mg/L administered for 4 hours, all 6 test rats died within 24 hours of administration. At an airborne concentration of about 0.04 mg/L, 3 of 6 test rats died within 24 hours and the remaining rats recovered without apparent ill effects. At levels of about 0.03 mg/L and below no mortality was observed. Pathological examination of the rats is underway, but at this time [the submitting company] is not in a position to further characterize or interpret the test results."

The submitter stated that "in view of the above results, a portion of the sample used in the inhalation test was administered intravenously to rats." It was reported that "no effects were noted until doses high enough to produce emboli were reached" and that the "high doses resulted in death." The submitter stated, however, that the "doses which approximated those which produced inhalation toxicity (assuming 100% absorption) produced no mortlity." In addition, the company stated that "the aliphatic carbamate had previously been found to have low oral toxicity (ALD greater than 25 g/kg) and only slight skin irritation and mild eye irritation."

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Submission Evaluation

Although the reported acute rat inhalation study results are preliminary and only a few animals were used in the study, the observed lethality was found to be dose-related. Other than the lethality, no other adverse effects were reported as being noted during the course of exposure or during the post-exposure period. In order to interpret the significance of the reported findings, EPA should request a complete copy of the final report and a complete copy of the results from the pathologic examination which is reported by the submitter to be underway. It is apparent that the submitting company was attempting to assess a "worst-case" exposure by testing a dust that was 99% respirable. The company reported that the typical exposure to the chemical would not be expected to involve dust particles that small.

It is of particular interest that the aliphatic carbamate was found to be more toxic (i.e., lethal) via the inhalation route than by intravenous administration. Without a complete copy of the final report (including test protocols and data) from the intravenous study, however, the validity of the results from the study cannot be determined.

If one assumes that the results of both the acute inhalation and intravenous studies are in fact valid, there are at least two hypotheses that may explain why the aliphatic carbamate was found to be more lethal via the inhalation route than when administered intravenously: 1) the inhaled material may have induced a rapid chemical pneumonitis resulting in pulmonary edema and/or may have affected pulmonary surfactant resulting in impaired oxygen uptake and/or carbon dioxide removal; and/or 2) the inhaled material may have caused bronchial constriction thereby shutting the airways. The second hypothesis is less tenable, however, unless the aliphatic carbamate and/or one of its metabolites reacted with the blood or its constituents. The results of the postmortem examination of the rats from the acute inhalation study should help to determine the validity of the above hyphotheses.

Current Production and Use

Due to the fact that the submitter has claimed the exact chemical identity of the tested material to be TSCA CBI, no information relating to production or use will appear in this status report. The submitting company did report, however, that a dust similar to that which was tested in the acute rat inhalation study would not be generated during the manufacture or end-use of the aliphatic carbamate.

Comments/Recommendations

The submitting company stated that although "a review of exposure during [aliphatic carbamate] manufacture indicates no exposure by the inhalation route," the company's employees were being advised about the submitted toxicologic findings. The submitting company also reported that it plans to conduct the following studies: 1) an industrial hygiene survey to "investigate the potential for inhalation exposures that could occur during manufacture, distribution and use of products containing aliphatic carbamate" and 2) other studies designed to define better the relationship between aliphatic carbamate particle size and possible toxicity. The submitting company stated that EPA would be notified about the status of the company's "scientific investigation of this problem and [about] any decisions as to changes, if any, in recommended industrial hygiene practices."

a) The Chemical Hazard Identification Branch (CHIB/AD/OTS) will request the submitting company to provide complete copies of the final reports (including test protocol(s) and data) from all of the toxicity studies cited in the company's submission.

b) The Chemical Hazard Identification Branch will screen the reported information to determine if further OTS assessment of the aliphatic carbamate is warranted.

c) The Chemical Hazard Identification Branch will send a copy of this status report to NIOSH, OSHA, CPSC, OW/EPA, OSWER/EPA, OANR/EPA, and ORD/EPA. A copy of this status report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0983-0493 S
Page 1 of 3

DATE: NOV 9 1983

SUBJECT: Status Report* 8EHQ-0983-0493 S

FROM: Justine L. Welch, Team Leader
Chemical Selection and Profiles Team/CSB

TO: Frank D. Kover, Chief
Chemical Screening Branch/ECAD/OTS

Approved 11/14

Revision Needed ______

Submission Description

The submitting company (name claimed to be TSCA Confidential Business Information (CBI)) reported that it was recently informed by one of its customers that three (3) of the customer's workers had exhibited "flu-like symptoms" after they had handled new and spent lots of a product identified non-confidentially by the submitter as a "mixture of metallic oxides." According to the submission, the submitting company "received no verification as to whether those symptoms were caused by exposure to [the submitter's] material nor as to whether the material was handled properly."

Submission Evaluation

Other than the statement that three workers had exhibited "flu-like symptoms" after handling new and used lots of the subject product, the submission did not present any further information about the actual condition of the affected workers. For example, the submission did not indicate whether the observed symptoms were serious, long-lasting, or incapacitating to any degree. In addition, no information was provided concerning the duration of the worker's exposure to the product, the time to onset of the observed symptoms, or the identity of other chemical substances to which the affected worker's were exposed that could have caused "flu-like symptoms." It should also be noted that the submitter did not report the chemical identity of the metallic oxide components of the subject mixture.

Current Production and Use

Considering the fact that the submitting company has claimed the exact chemical identity of the subject product to be TSCA CBI and did not report the actual chemical identity of the consituents of the product, no information concerning production or use of the product or its constituents will appear in this status report.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

EPA FORM 1320-6 (REV. 3-76)

Comments/Recommendations

It is the Agency's initial position that the acute human toxicity information, as presented in this submission, did not warrant reporting under section 8(e) of TSCA. The basis for the Agency's position is as follows:

> According the Part V of EPA's March 16, 1978 TSCA section 8(e) policy statement ("Statement of Interpretation and Enforcement Policy; Notification of Substantial Risk" 43 FR 11110), a "substantial risk of injury to health...is a risk of considerable concern because of (a) the seriousness of the effect...and (b) the fact or probability of its occurrence." With regard to the seriouness of the effect, EPA considers the human health effects for which substantial risk information must be reported to include "any instance of cancer, birth defects, mutagenicity, death or serious or prolonged incapacitation, including the loss of or inability to use a normal bodily function with a consequent relatively serious impairment of normal activities if one (or a few) chemical(s) is strongly implicated. In addition, Part VI(2) of the 8(e) policy document states that it is possible that effects less serious than those described above may be preliminary manifestations of those more serious effects and together with another triggering piece of information, constitute section 8(e)-reportable information.

Therefore, because the human health effects reported in this submission do not appear to be serious and do not appear to have resulted in a prolonged incapacitation or a serious impairment of normal bodily functions/activities, the Agency believes that the reported acute human toxicity information, when considered alone, did not warrant submission under section 8(e) of TSCA. It must be emphasized, however, that EPA's position with regard to the 8(e)-reportability of the submitted information is based solely on the provided information and not on pertinent information that may have been available to and/or considered by the submitter in deciding to report the observed symptoms under section 8(e).

It is also important to point out that although EPA does not believe that the human health effects information, as presented in this submission, was required for reporting pursuant to TSCA section 8(e), EPA does believe that as of November 21, 1983 (as explained below), such information may constitute an "allegation of a significant adverse reaction" as defined under TSCA section 8(c). Section 8(c) requires that "any person who manufactures, processes, or distributes in commerce any chemical substance or mixture" must keep "records of significant adverse reactions to health or the environment, as determined by the Administrator by rule, alleged to have been caused by the substance or mixture." Section 8(c) also requires that allegations of adverse reactions to the health of employees be kept for 30 years, and all other allegations be kept for five years. In addition, the Agency is empowered to inspect and/or require submission of 8(c) records.

On August 22, 1983, the Agency published (48 FR 38178) the final rule implementing section 8(c) of TSCA. Subject persons will be required to be in full compliance with section 8(c) of TSCA as of November 21, 1983.

a) In light of the preceeding discussion, the Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will transmit a copy of the August 22, 1983 Federal Register (48 FR 38178) notice on TSCA section 8(c) to the submitting company. In addition, the Chemical Screening Branch will request the submitting company to provide its rationale as to why the provided human health effects information was reported to the Agency under section 8(e) of TSCA. The Chemical Screening Branch will also request the submitter to provide the exact identity (including the CAS Registry Number if known) of each of the chemical components in the "mixture of metallic oxides." Considering EPA's general interest in company actions that are taken in response to chemical toxicity and exposure information, the Chemical Screening Branch will ask the submitter to describe the actions that have been taken or are planned by the submitter's company to determine the severity of the reported human toxicity and to determine the cause(s) of that toxicity.

NOTE: The submitter has been requested in writing by the OTS Document Control Officer to substantiate all of the company's confidentiality claims.

b) Copies of this status report will be sent to NIOSH and OSHA and to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-1083-0494
Page 1 of 4

DATE: NOV 21 1983

SUBJECT: Status Report* 8EHQ-1083-0494

Approved 11/21

Revision Needed ____________

FROM: Justine L. Welch, Section Chief
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD

Submission Description

Pursuant to Section 8(e) of TSCA, PPG Industries, Inc. provided to EPA's Office of Toxic Substances the summarized results of several in vivo toxicity studies of sodium azide (CAS No. 26628-22-8) and potassium azide (CAS No. 20762-60-1) According to PPG, the preliminary and final reports of the subject studies were previously submitted (in 1981) to the Office of Pesticide Programs (OPP/OPTS/EPA) under Section 6(a)(2) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) because the company had obtained a "registration for a formulating use of sodium azide." The following information was contained in the cover letter to PPG's April 14, 1981 FIFRA Section 6(a)(2) submission on sodium azide:

> "PPG Industries, Inc. has been pursuing the development of sodium azide for use as a soil fungicide. Several Experimental Use Permits have been obtained for its use on peanuts, rice, Florida vegetables and ornamentals. In 1974, a registration for a 15% granular formulation of sodium azide was issued (748-219) for formulating use only. Although this registration and these permits have had the effect of limiting environmental exposure to sodium azide to a minimum, nevertheless [PPG feels] compelled under Section 6(a)(2) of FIFRA to bring the following facts to [EPA's] attention:
>
> 1) There are several literature references to observed effects on the central nervous system due to exposure to sodium azide via intravenous or intraperitoneal injection in species such as rats and monkeys. (Casarett, L. J. and Doull J., Toxicology, The Basic Science of Poisons, pp 152-167 Macmilian (1975))
>
> 2) In 1970, as part of PP 1-G1066, PPG submitted a 125-Day Subacute Oral Toxicity Study of Potassium Azide [KN] on Beagle Dogs...In this study, animals were dosed with 0.1,

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

EPA FORM 1320-6 (REV. 3-76)

1.0 and 10.0 mg KN per Kg of body weight per day. At the high dose rate, symptoms of motor ataxia were observed in four of the eight treated animals. Two of these animals had to be sacrificed in extremis (a male after 60 days and a female after 111 days). However, no histopathological or other abnormalities were noted in this study. Subsequently, PPG has not been able to validate this study, largely because of [the company's] inability to track the individual animals in the raw data.

3) In 1980, PPG commissioned another subchronic oral feeding study in dogs...using [sodium azide] treatment rates of 1, 3 and 10 mg/Kg/day. In the 27th and last week of this study, ataxia was again observed in two high-dose females and one mid-dose male. However, unlike the earlier study, a draft report...indicates that compound-related histomorphologic changes were found in the two ataxic high-dose females. Lesions were detected in both the anterior and middle cerebral sections, and consisted of one or more of the following alterations: gliosis, vascular prominence due to endothelial cell swelling and condensation of the neuropil, demyelination and degenerative changes in the caudate nucleus. To the best of [PPG's] knowledge, this is the first time that CNS lesions have been found in animals treated by oral ingestion of sodium azide.

[The performing laboratory scientists] also reported possibly [sodium azide] treatment-related clinical chemistry findngs, including: decreased alkaline phosphatase in all male treated groups and in most female groups, decreased LDH levels in all male treated groups and decreased serum glutamic oxalocetic transaminase levels in most treated groups....

Other than the above, there were no distinct treatment-related trends evident in any of the body weight and food consumption data, opthalmologic and neurologic examinations, or the hematology, urinanalysis, gross pathology, terminal body weight and absolute and relative organ weight data."

In the cover letter to its Section 8(e) notice, PPG Industries, Inc. gave the following rationale for its decision to re-submit the toxicity information at this time under Section 8(e) of TSCA:

> "[PPG has] noted from recent press accounts that there are renewed plans for the production of air bag restraint systems for automobiles. [PPG] information in past years was that sodium azide is used as a propellant for air bags. In view of this possible expanded use, [PPG] thought it appropriate to make sure that the Office of Toxic Substances was aware of the information previously provided and [is] resubmitting the correspondence pursuant to Section 8(e)..."

Submission Evaluation

The results of the subchronic sodium azide feeding study in dogs are consistent with the results of other sodium azide studies in other species by other routes of exposure. The potency of sodium azide via the oral route appears to be similar to that found by either intraperitoneal or intramuscular injection. Although no histopathological abnormalities were observed in dogs exposed to potassium azide, the ataxia which was found is consistent with sodium azide toxicity; further potassium azide dosing might have resulted in overt pathology. Finally, the changes observed in both subchronic studies appear to be treatment related.

Current Production and Use

A review of the production range (includes importation volumes) statistics for sodium azide (CAS No. 26628-22-8), which is listed in the initial TSCA Inventory, has shown that between 20 thousand and 200 thousand pounds were reported as produced and/or imported in 1977. This production range information does not include any production/importation data claimed as confidential by those person(s) reporting for the TSCA Inventory, nor does it include any information that would compromise TSCA Confidential Business Information. **/

A review of the production range (includes importation volumes) statistics for potassium azide (CAS No. 20762-60-1), which is listed in the initial TSCA Inventory, has shown that no 1977 production/importation was reported or that all of the production range data reported were claimed as confidential by the manufacturer(s) and/or importer(s) and cannot be disclosed (see Section 14(a) of TSCA, U.S.C. 2613(a)). **/

In addition to the fungicidal applications cited in the Section 8(e) notice, sodium azide is used as an intermediate in organic syntheses and explosives manufacture, as a laboratory reagent for preserving solutions, and in preparing hydrazoic acid, lead azide and pure sodium. No information on the use(s) of potassium azide was located in the secondary literature sources consulted.

Comments/Recommendations

Technically, the provided toxicity information on sodium azide, once formally submitted to EPA under Section 6(a)(2) of FIFRA, need not have been submitted pursuant to Section 8(e) of TSCA. According to Part VII(b) of the Agency's March 16, 1978, TSCA Section 8(e) policy statement ("Statement of Interpretation and Enforcement Policy; Notification of Substantial Risk" 43 FR 11110), information need not be reported under TSCA Section 8(e)

**/ All data submitted for the TSCA Inventory, including the production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

if it "has been submitted in writing to EPA pursuant to mandatory reporting requirements under TSCA or any other authority administered by EPA (including the Federal Insecticide, Fungicide and Rodenticide Act...)."

A Chemical Hazard Information Profile (CHIP) on sodium azide was prepared by OTS staff on August 1, 1977.

a) The Chemical Screening Branch (CSB/ECAD/OTS) will screen the reported information in order to determine if further OTS assessment of sodium azide and/or potassium azide is warranted.

b) Considering the issue relating to the use of sodium azide as an air bag propellant, the Chemical Screening Branch will provide a copy of this status report to the Office of Motor Vehicle Safety Standards/National Highway Traffic Safety Administration/Department of Transportation (DOT). In addition, copies of this status report will be sent to NIOSH, OSHA, CPSC, FDA, DOT, OW/EPA, OSWER/EPA, OANR/EPA, ORD/EPA, and OPP/OPTS/EPA. A copy of this report will also be provided to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-1083-0495
Page 1 of 3

DATE: NOV 28 1983

SUBJECT: Status Report* 8EHQ-1083-0495

Approved 11/28

Revision Needed ____________

FROM: Justine L. Welch, Section Chief
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The Eastman Kodak Company submitted the final results/reports from an in vitro mammalian cell transformation assay and three in vitro Ames Salmonella typhimurium (bacteria) assays of 2-amino-4-phenylphenol (CAS No. 1134-36-7). Eastman Kodak provided the following summary of results in its submission:

> "On October 4, 1983, 2-amino-4-phenylphenol was reported to be positive in an In Vitro Mammalian Cell Transformation Assay by the Health, Safety, and Human Factors Laboratory of Eastman Kodak Company. The cell line was Balb 3T3 clone A31-1-13. This material induced foci of transformed cells over a concentration range of 1.2 ug/mL to 12 ug/mL. The relative cell survival covered by this concentration range was 99.5% to <1%. A statistically significant ($p<0.01$) increase in the frequency of transformed foci was observed at the 5 ug/mL and 12 ug/mL doses when compared to the solvent and untreated control cultures. These concentrations correspond to 50.6% and <1% relative cell survival. Based on these results 2-amino-4-phenylphenol is active in the In Vitro Balb 3T3 Cell Transformation Assay
>
> In July, 1975, [a contract laboratory] reported that the test compound was inactive in the Bacterial Mutagenesis Assay (Ames Test) for both activation and non-activation assays; however, the protocol used a single concentration (50 ug/mL per plate) and nine activation systems
>
> The compound was tested by the Eastman Kodak Company in the Bacterial Mutagenesis Assay (Ames Test) in 1977 and in 1980 The compound was weakly active with and without S-9 activation."

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Submission Evaluation

The provided in vitro genotoxicity results show that 2-amino-4-phenylphenol induces cellular transformation in Balb/c-3T3 cells when tested without metabolic activation. Although it was stated in the report that the chemical also induced gene mutation in Salmonella typhimurium strain TA 100 when tested both with and without metabolic activation in an S. typhimurium/mammalian microsomal assay (Ames test), no data were presented to support this claim. In light of this statement, and in the absence of evidence to the contrary, 2-amino-4-phenylphenol should be considered to be a bacterial mutagen. The negative results reported for this agent in the 1975 Ames assay must be discounted because strain TA 100 was not yet available for use in the assay and because only one minimal dose was tested.

In its submission, the Eastman Kodak Company also provided a Toxicity and Health Hazard Summary, Environmental Safety Data Sheet, and a report entitled, "Basic Toxicity of 2-Amino-4-Phenylphenol." According to the these reports, the acute oral LD50 for 2-amino-4-phenylphenol was found to be 2262 mg/kg in both rats and mice, and the acute dermal LD50 was found to be in excess of 1000 mg/kg in guinea pigs. In addition, the chemical was reported to be only slightly irritating to the skin (guinea pigs) and eyes (rabbits). The sensitization potential in guinea pigs was reportedly found to be moderate and the results of an 11-day feeding study in rats showed that the kidney and red blood cells were the major sites of toxicity.

Current Production and Use

A review of the production range (includes importation volumes) statistics for 2-amino-4-phenylphenol (CAS No. 1134-36-7), which is listed in the initial TSCA Inventory, has shown that between 1 thousand and 10 thousand pounds of this chemical substance were reported as produced/imported in 1977. This production range information does not include any production or importation data claimed as confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information which would compromise Confidential Business Information. The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

The following exposure/use information for 2-amino-4-phenylphenol was presented by Eastman Kodak in its submission:

> "Essentially all of the small amount of 2-amino-4-phenylphenol manufactured is used as a site-limited chemical intermediate by Eastman Kodak Company. This chemical is manufactured in closed equipment with potential for dermal and inhalation exposure only during a rotary drying operation. During this operation four operators are potentially exposed for 20 minutes/day up to 10 times/year. Their 8-hr

TWA exposure would be less than 1 mg/m^3 Worker exposure is minimized by local exhaust, use of neoprene gloves, safety glasses, and dust masks, and clothing is supplied and laundered by the corporation.

During on site use in closed equipment, dermal and inhalation exposure may occur for one to three people for 30 minutes/day up to 3 times/year. Local and general exhaust, dust masks, gloves, safety glasses, and protective clothing are used to minimize exposure. Potential exposure is estimated at less than 1 mg/m^3 8-hr TWA.

Less than 0.1% of the small amount manufactured is sold for laboratory use in 25 g bottles. One employee is involved in bottling. The operation occurs with local exhaust. Potential exposure may be 15 minutes/day, 1 day/year and is expected to be less than 1 mg/m^3 for the 15 minute operation.

Wastes from manufacture, use, and bottling are incinerated on site or treated in an on site activated sludge wastewater treatment facility; therefore, there is minimal risk to the environment from the manufacture, use, and processing of this chemical."

Comments/Recommendations

Although Eastman Kodak stated that the company was not aware of any adverse health problems associated with exposure to 2-amino-4-phenylphenol, the company did report that it is reviewing the current label and recommended handling procedures.

a) The Chemical Screening Branch (CSB/ECAD/OTS) will screen the reported toxicity and exposure information in order to determine the need for further OTS assessment of 2-amino-4-phenylphenol.

b) The Chemical Screening Branch will send a copy of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA and ORD/EPA. A copy of this status report will also be provided to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: NOV 23 1983

SUBJECT: Status Report* 8EHQ-1083-0496

Approved 11/28

Revision Needed ______

FROM: Justine L. Welch, Section Chief
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The Eastman Kodak Company submitted the final results from three in vitro mouse cell transformation assays, an in vitro mouse cell mutagenicity assay and two Ames/Salmonella typhimurium (bacteria) assays of 4-methyl-2-nitroaniline (CAS No. 89-62-3). Eastman Kodak provided the following summarized information in the cover letter to the company's submission:

> "On October 4, 1983, 4-methyl-2-nitroaniline was reported to be positive in an In Vitro Mammalian Cell Transformation Assay by the Health, Safety, and Human Factors Laboratory of Eastman Kodak Company. The cell line was Balb 3T3 clone A31-1-13. The three highest doses of 4-methyl-2-nitroaniline induced a statistically significant increase ($p<0.01$) in the number of transformed foci compared to the solvent or [the] untreated control cultures. The results suggest a dose response over the 50 ug/mL to 220 ug/mL concentration range. The survival at the five treatment doses ranged from 87.2% at 15 ug/mL to 31.5% at 220 ug/mL. These results indicate that 4-methyl-2-nitroaniline is active in the In Vitro Balb 3T3 Cell Transformation Assay
>
> In February, 1980, [a contract laboratory] reported that the test material induced significant increases in the number of transformed foci in the In Vitro Balb 3T3 Cell Transformation Assay (clone I13 C14) over the applied concentration range of 0.01 ug/mL to 20.0 ug/mL. This range corresponded to approximately 50% to 80% survival in the cytotoxicity test. The material was considered to be active in the In Vitro Balb 3T3 Cell Transformation Assay

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

In August, 1980, [the contract laboratory] reported that the test material did not induce transformed foci in the In Vitro Balb 3T3 Cell Transformation Assay (clone I13 C14) over the applied concentration range of 0.1 ug/mL to 25.0 ug/mL. This range corresponded to approximately 50% to 80% survival in the cytotoxicity test. The test material was considered to be inactive in the In Vitro Balb 3T3 Cell Transformation Assay.

A mutagenicity evaluation of 4-methyl-2-nitroaniline in the Mouse Lymphoma Forward Mutation Assay, completed by [the contract laboratory] in October, 1979, resulted in a significant increase in the mutation frequency at the TK locus in L5178Y Mouse Lymphoma cells only in the presence of rat liver S-9 microsomal activation. Concentrations from 31.3 ug/mL to 250 ug/mL were moderately toxic and induced dose-dependent increases in mutation frequency while 500 ug/mL was lethal. Without activation, concentrations up to the highly toxic level of 500 ug/mL were not detectably mutagenic. The compound was considered to be active in the presence of microsomal metabolism in the Mouse Lymphoma Forward Mutation Assay.

The material was found to be negative in the Bacterial Mutagenesis Assay (Ames Test) by [the contract laboratory] and by Eastman Kodak Company."

Submission Evaluation

There is no evidence from the submitted test data that 4-methyl-2-nitroaniline is a bacterial mutagen when tested in the Ames *Salmonella typhimurium* assay.

4-Methyl-2-nitroaniline was tested for its ability to induce morphologic transformation of Balb/c-3T3 cells on three occasions; once by Eastman Kodak and twice by a contract laboratory. The assay conducted by Eastman Kodak and one of the two assays conducted by the contract laboratory was positive; the other cell transformation assay conducted by the contract laboratory was negative. A review of the submitted data revealed no apparent reasons for this discrepancy. In light of the two positive responses, however, 4-methyl-2-nitroaniline should be considered to induce morphologic transformation in Balb/c-3T3 cells.

4-Methyl-2-nitroaniline was also tested for its ability to induce gene mutation in cultured mouse lymphoma L5178Y cells. Under the conditions of this test, the chemical was shown to be mutagenic for L5178Y cells when tested with metabolic activation. Although there is a discrepancy in the requirement for metabolic activation in the Balb/c-3T3 and mouse lymphoma L5178Y cell systems, it may be a reflection of the different inherent metabolic capabilities of these two cell lines. 3-Methylcholanthrene, for example, which requires metabolic activation when tested in the Ames assay and L5178Y cells, is a direct-acting transformant for Balb/c-3T3 cells.

In addition to the in vitro genotoxicity data, the Eastman Kodak Company also submitted a "Toxicity and Health Hazard Summary" for 4-methyl-2-nitroaniline. According to provided in vivo toxicity information, the acute oral LD50 for the compound was found to be approximately 1900 mg/kg in rats and in excess of 3200 mg/kg in mice. In addition, the chemical was found to cause slight eye irritation in rabbits and slight skin irritation (with no evidence of skin absorption) in guinea pigs. The provided information also indicates that 4-methyl-2-nitroaniline did not produce significant methemoglobinemia in rats dosed orally at 1000 mg/kg.

Current Production and Use

A review of the production range (includes importation volumes) statistics for 4-methyl-2-nitroaniline (CAS No. 89-62-3), which is listed in the initial TSCA Inventory, has shown that between 200 thousand and 2 million pounds of this chemical were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed as confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information which would compromise TSCA Confidential Business Information. The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

The Eastman Kodak Company reported that because the company does "not manufacture, process, or distribute [4-methyl-2-nitroaniline] in commerce...there is no employee exposure and no environmental release." Eastman Kodak also reported that "the chemical was last purchased and used in 1981 and there are no plans for future use."

Comments/Recommendations

In its submission, Eastman Kodak stated that although the company was "not aware of any adverse health problems associated with [4-methyl-2-nitroaniline]...any future use would be after careful review of the laboratory findings and handling procedures to assure maximum safety to personnel and the environment before working with the chemical."

a) The Chemical Screening Branch will screen the reported toxicity and exposure information in order to determine if further OTS assessment of 4-methyl-2-nitroaniline is warranted.

b) The Chemical Screening Branch will send a copy of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA and ORD/EPA. A copy of this status report will also be provided to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-1083-0497
Page 1 of 4

DATE: NOV 23 1983

SUBJECT: Status Report* 8EHQ-1083-0497

Approved Jk 11/23

Revision Needed

FROM: Justine L. Welch, Section Chief
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Chief
Chemical Screening Branch/ECAD

Submission Description

E. I. Du Pont de Nemours & Company, Inc. submitted summarized preliminary findings from a two-year rat inhalation study of titanium dioxide (CAS No. 13463-67-7) conducted at Du Pont's Haskell Laboratory for Toxicology and Industrial Medicine. According to Du Pont, 100 male and 100 female Charles River-CD rats were exposed to respirable titanium dioxide dust levels of 0, 10, 50 or 250 mg/m^3 for six hours per day, five days per week for 104 weeks. The titanium dioxide particles in the exposure chamber were reported to have had an estimated mass median diameter of approximately 1.6 microns. Du Pont reported that there were no effects on survival and no clinical signs of any adverse effect at any dose for rats exposed for 104 weeks. Du Pont also stated that no tumors were observed at any dose among the small number of rats sacrificed at three months, six months and one year. With regard to the remaining animals, Du Pont presented the following information:

> "The remaining rats were sacrificed at the end of the 104-week exposure period. All major tissues and organs were studied. All except the respiratory system were normal. In the lungs a preliminary diagnosis indicated a statistically significant incidence of microscopic tumors identified as squamous cell carcinoma (in about 10% of the rats) and bronchiolalveolar adenoma (in about 15% of the rats) at the 250 mg/m^3 level. No increased incidence of these tumors was observed at lower dose levels. In addition, although upon gross examination the rats appeared normal, the tissues lining the nasal cavity and the trachea showed microscopic evidence of irritation. Minute areas of lung fibrosis were also noted at the two higher exposure levels."

Du Pont reported that the titanium dioxide respirable dust level of 250 mg/m^3 (i.e., the dose level producing tumors in rats) is well above that which could be obtained in an occupational setting. Du Pont also reported that a survey of personal monitoring data from Du Pont plants indicated "that in the job with the highest potential for exposure, the highest mean exposure was 3.1 mg/m^3 of total dust with a range of 0.7 to 3.1 mg/m^3." Based on these preliminary measurements, Du Pont stated that "the maximum respirable fraction is 42% of the total dust."

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

As background information, Du Pont reported that titanium dioxide "is essentially nontoxic on an acute basis, as its approximate lethal oral dose is greater than 25 g/kg." Du Pont also reported that titanium dioxide was tested by the National Cancer Institute (NCI) at 25,000 or 50,000 ppm in the diets of Fisher 344 rats and B6C3F1 mice for 103 weeks and was not found to be carcinogenic in either species (DHEW Publication No. 79-1347 (NIH)).

In conclusion, Du Pont stated that the information presented in its submission does "not suggest that existing manufacturing practices in the titanium dioxide industry or use by customers poses risk of adverse health effects."

Submission Evaluation

Titanium is not known to be a carcinogenic metal. As reported by the submitter, the NCI 2-year feeding study with rats and mice showed that titanium dioxide was non-carcinogenic under the conditions of the bioassay. The findings of this NCI bioassay are consistent with the results of earlier studies in which titanium itself failed to display tumorigenicity. The small percentage of pulmonary squamous cell carcinomas and bronchioalveolar adenomas observed at the high dose (i.e., 250 mg titanium dioxide pigment dust/m^3) in Du Pont's 2-year rat inhalation study may be ascribed to the pneumoconiosis-inducing properties of hard mineral dusts. Silicosis is the most extensively studied type of pneumoconiosis and it is known that in a small percentage of cases, the resulting fibrotic tissue may give rise to malignant lung tumors.

Current Production and Use

A review of the production range (includes importation volumes) statistics for titanium dioxide (CAS No. 13463-67-7), which is listed in the initial TSCA Inventory, shows that between 500 million and 1.8 billion pounds were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed as confidential by those persons reporting for the TSCA Inventory, nor does it include any information which would compromise TSCA Confidential Business Information. The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

According to secondary literature sources, titanium dioxide can be used in the production of white pigment in paints, paper, rubber, and plastics; as an opacifying agent; in cosmetics; radioactive decontamination of skin; floor coverings; glassware and ceramics; enamel frits; delustering synthetic fibers, printing inks and welding rods.

Comments/Recommendations

In its submission, Du Pont stated that the current OSHA Standard for titanium dioxide (as a "nuisance dust") is 15 mg/m^3 and the American Conference of Governmental Industrial Hygienists (ACGIH) has recommended a titanium dioxide Threshold Limit Value (TLV) of 10 mg/m^3. According to Du Pont, the high dose level (250 mg/m^3) of titanium dioxide respirable dust which was tested in the company's two-year rat inhalation study, in addition to being well above both the OSHA Standard and ACGIH TLV, is also well above that which could be obtained in an occupational setting. Nevertheless, Du Pont stated that in view of the reported oncogenicity findings, the company plans to:

1. communicate the test results and Du Pont's assessment of their meaning to employees, competitors and customers, and to other Federal agencies (OSHA, NIOSH, FDA and MSHA);

2. conduct an epidemiology or detailed employee health study; and

3. assess the need for further toxicity studies.

With regard to its plans to conduct an epidemiology or employee health study, Du Pont stated that although preliminary indications are that the employees in Du Pont's titanium dioxide manufacturing plants have experienced no statistically significant increase in incidence of mortality from lung cancer, the company plans to confirm these findings. Du Pont also reported that the company will advise EPA of the results of further Du Pont studies and will provide to EPA a final report of the 2-year rat inhalation study with titanium dioxide as soon as that report becomes available.

There a number of titanium dioxide-related actions/activities that are underway within and/or completed by the other EPA Program Offices under such authorities as the Clean Water Act (CWA), the Clean Air Act (CAA), and the Resource Recovery and Conservation Act (RCRA).

a) The Chemical Screening Branch (CSB/ECAD/OTS) will request E. I. Du Pont de Nemours & Company, Inc. to ensure that EPA receives a complete copy of the final report from Du Pont's 2-year titanium dioxide inhalation study including test protocols and data. In addition, Du Pont will be requested to provide to EPA any available information with regard to the job or job categories with the highest potential for occupational exposure to titanium dioxide.

b) The Chemical Screening Branch will screen the submitted information on titanium dioxide in order to determine the need for further OTS assessment.

c) The Chemical Screening Branch will transmit copies of this status report to NIOSH, OSHA, MSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA, ORD/EPA, and OPP/OPTS/EPA. In addition, a copy of the report will be sent to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-1083-0498
Page 1 of 4

DATE: NOV 25 1983

SUBJECT: Status Report 8EHQ-1083-0498

Approved 11/25

Revision Needed ____________

FROM: Justine L. Welch, Section Chief
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The Gulf Oil Chemicals Company submitted final results/reports from a two-week repeated dose rat dermal toxicity study and a nine-day repeated dose rat inhalation toxicity study of Gulf Aromatic Pyrolysis Oil (CAS No. 64742-90-1). The submitter's cover letter presented the following summarized results:

> "There were no animal deaths reported in either study; however, there were several toxicological effects. In the two-week dermal toxicology study on rats, the material was applied to the backs of the rats at 2 dose levels, either 2 g/kg (undiluted) or 1 g/kg (diluted with corn oil) for 9 daily applications during a 14-day period. The test material was wiped from the backs of the animals approximately 6 hours after application. Findings related to dermal exposure to the test material included moderate to severe erythema with eschar formation, alopecia, peeling skin and dermal fissures. Hair loss was not seen in the low dose animals. Histological evaluation of the skin of the high dose animals showed hyperplasia, acanthosis and hyperkeratosis. Possible treatment-related effects included: depression of body weight gain and food consumption, and increased liver weight. There were no changes in the liver function as reflected in the blood chemistry profile nor were there any histopathological changes reported in the liver.
>
> In the inhalation study, rats were exposed to airborne concentrations of 0.5 g/M^3 or 2.0 g/M^3 of Aromatic Pyrolysis Oil, 6 hours/day for a total of 9 days during a 12-day period. Treatment-related effects resulting from inhalation exposure included body weight loss, yellow discoloration of the lungs, and hyperplasia of the alveolar macrophages. Significant changes occurred in several organ weights: liver and lung weights were increased, while spleen and heart weights were decreased. There were no biologically significant changes in the hematology or blood chemistry values."

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

With regard to the relevance of the performed subacute toxicity studies toward human health, the submitter stated that the company considered the following two items to be significant:

> "Firstly, in the dermal study, there was no attempt made to wash the material off the skin following exposure, as would occur in the workplace. Thus, the animals were exposed over a 6-hour period to a high concentration of the test material which covered approximately 10 percent of the body surface area. Secondly, in the inhalation study, the dose levels were 100-400 times the oil mist standard which would be used for an upper exposure limit in the workplace and does provide a reasonably high margin of safety."

In addition to the subacute in vivo toxicity studies, the company stated that a draft report of an in vitro BALB/3T3 Mouse Cell Transformation Test concluded that Gulf Aromatic Pyrolysis Oil was positive under the conditions of the test.

Submission Evaluation

The reported two-week repeated dose dermal toxicity and nine-day repeated dose inhalation toxicity studies indicate that Aromatic Pyrolysis Oil is toxic but not unusually so. Although exposures were reliably associated with various toxic symptoms/signs, including weight loss, ocular and nasal discharge, hair loss and skin reactions, the brain and lungs were only minimally affected; such is not the case with many hydrocarbon exposures. There was no mortality reported by either the dermal or inhalation routes of exposure. The observed skin fissuring and pulmonary alveolar macrophage hyperplasia are to be expected as similar adverse effects have been reported with dermal and inhalation exposures to other petroleum process steams. It is probably significant that microscopic examination of the lungs did not yield reports of macrophage necrosis or of polymorphonuclear infiltration in the lung. The skin effects resulting from inhalation exposure illustrate well that whole-body inhalation exposure involves dermal exposure. Apparently, inhalation exposure was more effective than dermal administration in eliciting a depression of spleen weight and an elevation of serum glutamic-pyruvic transaminase (SGPT), the latter in the high-dosage group. Although these changes were not dramatic and their biological importance is not clear, the SGPT observation does tend in a small way to weaken the conclusion in the Gulf cover letter that there were "...no changes in...liver function as reflected in the blood chemistry profile...." The increase seen in liver weights with exposure was probably reactive or adaptive, rather than pathological.

The submitted inhalation study highlights the importance of measuring the actual concentration of the test material in the exposure chamber, and preferably in the animals' breathing zone. In the low-dose group, the actual concentration measured in the chamber was only one-quarter of the nominal or estimated concentration (i.e., 0.54 g/M^3 actually present, compared with 2.2 g/M^3

calculated to be the nominal concentration). The difference was even more pronounced in the high dose group, in which the actual concentration was less than one-tenth of the nominal concentration (i.e., 2.0 g/M^3 actual versus 22.4 g/M^3 nominal).

Current Production and Use

A review of the production range (includes importation volumes) statistics for Gulf Aromatic Pyrolysis Oil (CAS No. 64742-90-1), which is listed in the initial TSCA Inventory, has shown that over 1.39 billion pounds were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed as confidential by those person(s) reporting for the TSCA Inventory, nor does it include any information which would compromise TSCA Confidential Business Information. The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

According to the definitions section of the TSCA Inventory, CAS No. 64742-90-1 pertains to steam-cracked petroleum residues which are defined as follows:

> "A complex combination of hydrocarbons obtained as the residual fraction from the distillation of the products of a steam cracking process (including steam cracking to produce ethylene). It consists predominantly of unsaturated hydrocarbons having carbon numbers predominantly greater than C14 and boiling above approximately 260°C (500°F). This stream is likely to contain 5 wt. % or more of 4- to 6-membered condensed ring aromatic hydrocarbons."

In its submission, the Gulf Oil Chemicals Company stated that its "Aromatic Pyrolysis Oil is an intermediate process stream from an ethylene/quench oil pyrolyis unit which is used for supplementary fuel for [Gulf's] olefins operations." With regard to exposure to this oil, the submitting company reported:

> "Generally, the material will be totally contained within piping, instruments, and process equipment. The only time the material is not totally enclosed is when filters and furnace burners are cleaned, or when drain lines are opened from sampling ports, pump seals, valve packings, and heat exchangers. The material also has negligible vapor pressure under normal operating temperature which minimizes the formation of airborne concentrations. Potential exposure to [company] employees is considered minimal, and no consumer exposure occurs since the material has not been introduced into commerce."

Comments/Recommendations

In the cover letter to its submission, the Gulf Oil Chemicals Company stated that although the company's "long-standing work practices, and current safety, health, and hygiene procedures provide adequate protection for the approximately 20 persons per shift who work in the process area," the company is revising the Gulf Aromatic Pyrolysis Oil Material Safety Data Sheet (MSDS), reviewing appropriate company industrial hygiene data, and notifying Gulf employees and potential customers about the results of the reported studies. The submitter also stated that the final report of the BALB/3T3 Mouse Cell Transformation Test will be provided to EPA when the report is received from the laboratory.

EPA's Office of Toxic Substances (OTS) has received and evaluated a number of TSCA Section 8(e) and "For Your Information" submissions containing toxicologic and/or exposure data on a variety of coal, shale, and petroleum oils, process streams, and/or wastes.

a) In view of EPA's general interest in corporate actions that are taken on a voluntary basis in response to chemical toxicity and/or exposure information, the Chemical Screening Branch (CSB/ECAD/OTS) will ask the Gulf Oil Chemicals Company if it is conducting, or has plans to conduct, additional laboratory studies designed to further define the toxicity of Aromatic Pyrolysis Oil.

b) The Chemical Screening Branch will screen the reported information to determine if further OTS assessment of this petroleum stream is warranted.

c) The Chemical Screening Branch will send a copy of this status report to NIOSH, OSHA, DOE, OW/EPA, OSWER/EPA, ORD/EPA, and OANR/EPA. A copy of this report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-1083-0499
Page 1 of 3

DATE: NOV 29 1983

SUBJECT: Status Report* 8EHQ-1083-0499

Approved 11/20

Revision Needed ________

FROM: Justine L. Welch, Section Chief
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

Vulcan Chemicals submitted copies of abstracts from two male rat reproduction studies of chloromethane (methyl chloride; CAS No. 74-87-3) that were conducted at the Chemical Industry Institute of Toxicology (CIIT). According to Vulcan, the results of the performed studies show that chloromethane produced "a strong but reversible dominant lethal effect in the male F-344 rat, as well as a lowered sperm number and motility in exposed animals." The submitted abstracts follow:

"A DOMINANT LETHAL STUDY OF INHALED METHYL CHLORIDE IN MALE F-344 RATS. P.K. Working, J.S. Bus, R.M. Norton and T.E. Hamm, Jr., Chem. Indus. Inst. Toxicol., Research Triangle Park, NC 27709.

"The genotoxic effect of inhaled methyl chloride (MeCl), a known testicular toxicant, was assessed in a dominant lethal test (DLT) using male F-344 rats. Four groups of 40 males were exposed to 0, 1000 or 3000 ppm MeCl 6 hr/day for 5 days or received an ip injection of triethylenemelamine (TEM, 0.2 mg/kg) on the afternoon of day 5 as a positive control. After a 2 day recovery period, an F-344 female was caged with each male weekly for 8 weeks. Necropsy of females was 17 days after the first day of cohabitation. Exposure to 0 or 1000 ppm caused no change in any DLT parameter measured. Exposure to 3000 ppm resulted in sperm granulomas in one or both of the epididymides of 39% of the males. TEM caused increases in both dead implants/total implants (D/T, up to 0.98) and preimplantation loss (PI loss, up to 7.3/-female) only at weeks 1 to 5 post-exposure (PE), indicative of a strong dominant lethal effect and subsequent recovery. 3000 ppm MeCl caused slight increases in D/T only at weeks 1 and 2 PE (0.17 and 0.33 respectively), and increases in PI loss (up to 9.1/female) during all 8 weeks. Pregnancy rate was decreased at every week PE, ranging from 28-78% (control range = 83-95%). [The authors] conclude that MeCl is an inducer of dominant lethal mutations in mature sperm exposed in the vas deferens and [the] epididymis."

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

"EFFECTS OF INHALED METHYL CHLORIDE ON SPERM OF F-344 RATS. P.K. Working, J.S. Bus, L.L. Earle and T.E. Hamm, Jr., Chem. Indus. Inst. of Toxicol., Research Triangle Park, NC 27709.

"In a dominant lethal test using male F-344 rats, 3000 ppm of inhaled methyl chloride (MeCl) increased post-implantation loss in weeks 1 and 2 post-exposure (PE), and increased pre-implantation (PI) loss and decreased pregnancy rate up to 8 weeks PE. [The authors] examined the cause of these changes in male F-344 rats exposed to 0, 1000 or 3000 ppm MeCl 6 hr/day for 5 days or after a single ip injection of 0.2 mg/kg triethylenemelamine (TEM). Five males per treatment were examined each week for 8 weeks PE. In the 3000 ppm-exposed males the testis/body weight ratio was decreased to 88% of control by week 3 PE and declined to 50% of control at week 8. In sperm isolated from the vas deferens, motility was decreased to 70% of control at 1 week PE and cell number was decreased to 52% of control by week 2. Both parameters continued to decline throughout the 8 wk observation period. Testicular spermatid count at week 8 (a measure of spermatogonial survival) was 22% of control levels and was depressed as early as 2 weeks PE, suggesting destruction of more mature spermatogenic stages. No effect of exposure to 1000 ppm MeCl or TEM was seen on any parameter measured. Thus, the increased PI loss and decreased pregnancy rate in females bred to 3000 ppm exposed males is due primarily to failure of fertilization because of lowered sperm number and motility."

Submission Evaluation

The evaluation of the reported and other toxic effects of chloromethane is being conducted by the Test Rules Development and Risk Management Branches within the Existing Chemical Assessment Division/OTS in conjunction with the Health and Environmental Review Division/OTS. Chloromethane was initially recommended in October 1977 by the Interagency Testing Committee (ITC) to EPA for testing consideration under Section 4 of the Toxic Substances Control Act. On July 18, 1980, the Test Rules Development Branch published (45 FR 48524) a proposed "test rule" for chloromethane carcinogenicity and teratogenicity testing. In addition, OTS is currently gathering additional exposure and toxicity information on chloromethane under TSCA Sections 8(a) and 8(d).

Current Production and Use

A review of the production range (includes importation volumes) statistics for chloromethane (methyl chloride; CAS No. 74-87-3), which is listed in the initial TSCA Inventory, has shown that between 281 million and 960 million pounds of this chemical were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed as confidential by those person(s) reporting for the TSCA Inventory, nor does it include any information which would compromise Confidential Business Information. The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710). According to information contained in the July 14, 1982 issue of Chemical & Engineering News, U.S. chloromethane production in 1981 was estimated to be 362 millions pounds.

According to secondary literature sources, chloromethane can be used as a catalyst carrier in certain types of polymerization reactions. Chloromethane can also be used in the manufacture of silicones, tetramethyl lead, synthetic rubber, methyl cellulose, refrigerants, fumigants, and certain organic chemicals (e.g., chloroform, carbon tetrachloride, methylene chloride). In addition, the chemical can be used as an extractant, a propellant and an herbicide.

Comments/Recommendations

In 1974, the Occupational Safety and Health Administration (OSHA) set the current occupational standard for chloromethane exposure at an 8 hour time-weighted average (TWA) of 100 parts per million (ppm) in air with a 200 ppm ceiling level (39 CFR 23540). In 1980, the ACGIH (American Conference of Governmental Industrial Hygienists) recommended a chloromethane threshold limit value (TLV) of 50 ppm in air.

In addition to the TSCA-related chloromethane actions/activities described in the Submission Evaluation section of this status report, Volume II of the June 1982 EPA Chemical Activities Status Report (EPACASR; EPA 560/TIIS-82-002b) indicates that there are a number of chloromethane actions/activities in other EPA Program Offices under such authorities as the Clean Water Act (CWA); the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA;"Superfund"); and the Resource Conservation and Recovery Act (RCRA). EPA's Office of Toxic Substances has also received and evaluated several other TSCA Section 8(e) and "For Your Information (FYI)" submissions containing toxicity and/or exposure data on chloromethane.

a) In view of EPA's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the Chemical Screening Branch (CSB/ECAD/OTS) will request Vulcan Chemicals to describe the actions the company has taken in light of the reported toxicity information on chloromethane to warn workers and others and to reduce and/or eliminate exposure to the chemical.

b) The Chemical Screening Branch will transmit a copy of this status report to NIOSH, OSHA, CPSC, FDA, OW/EPA, OSWER/ EPA, OANR/EPA, ORD/EPA, OPP/OPTS, TRDB/ECAD/OTS and RMB/ECAD/OTS. In addition, a copy of this status report will be transmitted to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-1283-0500 S
Page 1 of 2

DATE: DEC 22 1983

SUBJECT: Status Report* 8EHQ-1283-0500 S

Approved 12/23/83

Revision Needed

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Note

The submitting company has claimed its identity and the exact identity of the subject chemical substance to be TSCA Confidential Business Information (TSCA CBI) The OTS Document Control Office has requested the submitter to substantiate all of the company's confidentiality claims

Submission Description

The submitting company provided summarized final results from a battery of *in vitro* genotoxicity tests of a "substituted polyglycidyl benzenamine." According to the submitted information, the chemical was positive both in the presence and absence of exogenous metabolic activation in an Ames *Salmonella typhimurium* (bacteria) Mutagenicity Assay, an L5178Y Mouse Lymphoma Cell Forward Mutation Assay, and a Chinese Hamster Ovary (CHO) Cell Sister Chromatid Exchange (SCE) Assay. The chemical was also reported to be mutagenic in yeast (*Saccharomyces cerevisiae* strain D7) but only in the presence of metabolic activation.

Submission Evaluation

Although the submission did not contain any of the actual data from the performed genotoxicity studies, the experimental design reports and summary statements of results which were submitted do indicate that the substituted polyglycidyl benzenamine was positive in all of the cited assays. Considering that many compounds of this type have been shown to be genotoxic, there is no reason to assume that the submitted reports do not accurately reflect the obtained experimental findings. In order to ensure that this is the case, however, a complete copy of the final report, including the actual test protocol(s) and data, from each of the genotoxicity studies that were cited in the submission should be obtained for review.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information

Current Production and Use

Although the submitting company did not provide any information concerning the proposed use(s) of the substituted polyglycidyl benzenamine, it was reported that the chemical is currently in the research and development (R&D) stage and that the number of people potentially exposed to the chemical is very small. The submitter also reported that current exposures to the substituted polyglycidyl benzenamine are being controlled by good laboratory practices.

Comments/Recommendations

Although a positive genotoxicity test result, when considered alone, may not be sufficient to offer reasonable support for a conclusion of substantial risk, the Agency believes that such results are of value in assessing possible risks posed by chemicals to health and/or the environment. EPA also believes that positive genotoxicity test results in combination with additional information (e.g., knowledge of potential exposure to, or high production of, the chemical substance or mixture), would suggest, in many cases, the need to conduct additional toxicologic studies with the results of such studies considered for possible submission to the Agency pursuant to Section 8(e) of TSCA.

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will request the submitter to provide a complete copy of the final report (including the actual test protocol(s) and data) from each of the *in vitro* substituted polyglycidyl benzenamine genotoxicity assays that were cited in the submission. In addition, the submitting company will be requested to submit a structural diagram of the subject chemical. In view of the Agency's general interest in corporate actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the Chemical Screening Branch will also ask the submitting company if it is conducting or plans to conduct additional studies designed to further define the toxicity of the substituted polyglycidyl benzenamine.

b) The Chemical Screening Branch will screen the reported information to determine if further OTS assessment of the substituted polyglycidyl benzenamine is warranted at the present time.

c) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA, and ORD/EPA. A copy of this status report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-1283-0501 S
Page 1 of 3

DATE: JAN 9 1984

SUBJECT: Status Report* 8EHQ-1283-0501 S

Approved 1/10/84

Revision Needed ____________

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Note

The submitting company claimed its name and the exact identity and use category of the subject chemical substance to be TSCA Confidential Business Information (TSCA CBI). The OTS Document Control Officer has requested the submitter to substantiate all of the company's confidentiality claims.

(See note on Page 3 of this report.)

Submission Description

The submitting company provided summarized findings from two (2) acute rat toxicity studies of a chemical substance that was identified generically by the submitter as an acylcyclohexyldione. The following synopsis of the obtained results was presented in the submission:

> "In a preliminary evaluation of the acute oral toxicity of this material, graded doses ranging from 100 to 500 mg/kg were given to adult Sprague-Dawley rats of both sexes. At all levels, including 100 mg/kg (which dose was nonlethal to the animals), severe paralysis of the hind limbs was observed. In a dermal toxicity screen, rats were given doses of 2000 or 500 mg/kg. At 2000 mg/kg, 4/4 females and 3/4 males died. The survivor displayed signs of hindlimb weakness and decreased motor activity. At 500 mg/kg, no animals died, but 3/4 females and 1/4 males showed hindlimb weakness and decreased motor activity. In the case of those animals which did not die, the condition persisted until it became necessary to sacrifice the animals because of the nature of their conditions. A preliminary pathological examination of material from these animals indicates a direct effect upon the nervous system."

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Submission Evaluation

The submitted summarized information indicates that the observed development of severe and persistent paralysis following acute exposure to non-lethal doses of acylcyclohexyldione is the result of a direct neurotoxic effect rather than a behavioral phenomenon secondary to other systemic toxicity or general depression of the central nervous system. A complete copy of the final report from each of the acute toxicity studies cited in the submission should be requested in order to evaluate better the reported findings.

Current Production and Use

Although the submitting company has claimed the exact identity and use category of the subject chemical to be TSCA Confidential Business Information, the company did report non-confidentially that the chemical is "a research compound which is the fifth intermediate in a chain of seven, including the final product...."

(See note on Page 3 of this report)

Comments/Recommendations

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will request the submitting company to submit complete copies of the final reports (including test protocols and data) from the acute oral and dermal toxicity studies of the acylcyclohexyldione in rats. Considering EPA's general interest in company actions which are taken on a voluntary basis in response to chemical toxicity/exposure information, the Chemical Screening Branch will request the submitting company to describe the actions that it has taken which are designed to reduce and/or eliminate worker and other exposure to the subject chemical. The Chemical Screening Branch will also ask the submitting company to descibe the studies that the company has conducted, is presently conducting, or is planning to conduct that are designed to define better the toxicity of and/or exposure to acylcyclohexyldione.

b) The Chemical Screening Branch will screen the reported information to determine if further OTS assessment of the subject chemical is warranted at the present time.

c) The Chemical Screeing Branch will send copies of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA, and ORD/EPA. In addition, a copy of this status report will be transmitted to the TSCA Assistance Office (TAO/OTS) for further distribution.

NOTE:

In a non-confidential letter (dated January 24, 1984), the Chevron Chemical Company stated that the company had decided to withdraw its confidentiality claims for the information contained in the company's initial Section 8(e) submission. The declassified initial submission reported that the subject chemical is 2-(2-oxobutyl)-5-(2-ethylthio)-propyl-3-hydroxy-2-cyclohexen-1-one and that the CAS Registry No. was 79419-43-5. In addition, the initial 8(e) submission reported that "this research compound, which is the fifth intermediate in a chain of seven, including the final product, in the manufacture of a chemical that, if developed succcessfully, would be registered as a pesticide." The Section 8(e) submission also reported that although 2-(2-oxobutyl)-5-(2-ethylthio)-propyl-3-hydroxy-2-cyclohexen-1-one is produced in batches at the present time, "it is not known whether, in the final process, this material will be manufactured in batch mode, thereby isolating it, or whether it will be subject to a continuous manufacturing process." According to Chevron, "it is not known whether this intermediate will appear in the final product."

In its initial 8(e) submission, the Chevron Chemical Company also included a preliminary draft Material Safety Data Sheet (MSDS) which contains summarized findings from the company's acute toxicity studies of and recommended safe handling procedures for 2-(2-oxobutyl)-5-(2-ethylthio)-propyl-3-hydroxy-2-cyclohexen-1-one. According to Chevron, the MSDS has been distributed to Chevron employees who handle the chemical and "will be sent to potential toll manufacturers."

a) The Chemical Screening Branch (CSB/ECAD/OTS) will send a copy of this updated status report to each office listed in item c) on page 2 of this report and to EPA's Office of Pesticide Programs.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: JAN 27 1984

SUBJECT: Status Report* 8EHQ-1283-0502 P

Approved 1/31/84

Revision Needed ______

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The General Motors Corporation submitted information concerning a report from an employee of the Packard Electric Division (General Motors) that the fumes generated during the heating/molding of Hypalon Molding Compound are "very irritating" and "cause a burning sensation in the lungs, throat and nasal passages." In its submission, the General Motors Corporation provided 1) a copy of the employee's report; 2) summaries of internal General Motors and Packard Electric Division investigations, conclusions, and recommendations; 3) a list of the ingredients used to formulate the Hypalon Molding Compound; 4) copies of Material Safety Data Sheets (MSDSs) for each ingredient; and 5) the process specifications for the Hypalon molding operation. In the cover letter to its submission, the General Motors Corporation stated that the company believes that the irritation experienced by the employee may have been caused by aldehydes, hydrogen chloride, and/or sulfur oxides that originate from the thermal decomposition of Hypalon Molding Compound during the molding operation. General Motors also stated that the affected employee may be more sensitive to such irritants due to the fact that other workers exposed in a similar manner have complained only about the odors.

Submission Evaluation

General Motors' hypothesis that the reported irritation was due to aldehydes, hydrogen chloride (hydrochloric acid) and/or sulfur oxides is plausible but does not appear to be supported by data from actual monitoring of the workplace air, particularly the breathing-zone air around the molding operation. Considering the large number of ingredients used in the formulation of Hypalon Molding Compound and the high temperature (i.e., 400°F) required during part of the molding operation, it is not suprising that a wide variety of irritating substances (including those cited by the submitter) could be released. Although the General Motors Corporation contends that the affected worker (i.e., the Packard Electric Division employee who made the formal complaint) is unusually sensitive to thermal decomposition products of Hypalon

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Molding Compound (because other workers who are exposed in a similar manner have complained only about the odors), the General Motors Corporation's contention is not supported by a submitted Packard Electric Division investigative report which states that other workers involved in the Hypalon molding operation have made complaints similar to those issued by the affected worker. Although it is possible that the affected worker has a natural (or possibly acquired?) low tolerance to the thermal decomposition products of Hypalon Molding Compound, the fact remains that other employees are being exposed in a similar manner and have complained, even if only about the odors. It should be noted that chemical substances can, and in many cases, do elicit serious toxic effects (e.g., liver damage) at levels well below those which can be detected by smell or which cause overt irritation to skin, eyes, lungs, nasal passages, etc.

A submitted internal General Motors memorandum recommends that the company's Industrial Hygiene Department be consulted for an evaluation of the molding process environment. This recommended action appears to be prudent in view of the workers' complaints and the large number of chemicals to which the employees are potentially exposed during the molding operation. If the submitter is correct that hydrochloric acid and sulfur oxides are among the thermal decomposition products of Hypalon Molding Compound, the corrosive effects of these chemicals on the workplace ventilation system should be taken into account by the company. With regard to the existing ventilation system, the submission did not indicate whether air from the molding operation is directed through an air quality control system prior to release to the outside.

Current Production and Use

According to an engineering specification sheet contained in the submission, Hypalon Molding Compound, once formulated, is used to manufacture spark plug boots. Considering the nature of the submission, no information concerning the production and use of the individual ingredients used to formulate Hypalon Molding Compound or the reported (and other) thermal decomposition products of the Hypalon Molding Compound will be included in this status report.

Comments/Recommendations

It is EPA's initial position that the acute human toxicity information, as presented in this submission, did not warrant reporting under Section 8(e), the substantial risk information reporting provision of the Toxic Substances Control Act (TSCA). It should also be noted that a submitted report prepared by the General Motors Corporation's "Toxic Materials Control Activity" stated that a Section 8(e) notification was not necessary. The "Toxic Materials Control Activity" position was based on a review of the Hypalon molding process and the materials involved and a finding that no new or undocumented effects had been observed. The basis for EPA's position with regard to the Section 8(e)-applicability of the submitted information is as follows:

According the Part V of EPA's March 16, 1978, TSCA Section 8(e) policy statement ("Statement of Interpretation and Enforcement Policy; Notification of Substantial Risk" 43 FR 11110), a "substantial risk of injury to health...is a risk of considerable concern because of (a) the seriousness of the effect...and (b) the fact or probability of its occurrence." With regard to the seriousness of the effect, EPA considers the human health effects for which substantial risk information must be reported to include "any instance of cancer, birth defects, mutagenicity, death or serious or prolonged incapacitation, including the loss of or inability to use a normal bodily function with a consequent relatively serious impairment of normal activities if one (or a few) chemical(s) is strongly implicated. In addition, Part VI(2) of the 8(e) policy document states that it is possible that effects less serious than those described above may be preliminary manifestations of those more serious effects and together with another triggering piece of information, constitute Section 8(e)-reportable information.

In view of the above discussion and considering that the acute human health effects reported in this submission do not appear to have been serious or to have resulted in prolonged incapacitation or serious impairment of normal bodily functions/activities, EPA does not believe that the information warranted submission under Section 8(e) of TSCA. It must be emphasized, however, that the Agency's position with regard to the 8(e)-reportability of the subject information is based solely on the information submitted to EPA and not on other pertinent information that may have been available to and/or considered by the General Motors Corporation in the company's ultimate decision to submit the information to EPA under Section 8(e) of TSCA.

It is also important to note that although the Agency does not believe that the human health effects information, as presented in the General Motors submission, warranted reporting under TSCA Section 8(e), the Agency does believe that the employee's report could possibly constitute an "allegation of a significant adverse reaction" as defined under Section 8(c) of TSCA. Section 8(c) of TSCA requires that "any person who manufactures, processes, or distributes in commerce any chemical substance or mixture" must keep "records of significant adverse reactions to health or the environment, as determined by the Administrator by rule, alleged to have been caused by the substance or mixture." Section 8(c) of TSCA also requires that allegations of adverse reactions to the health of employees be kept for thirty (30) years, and all other allegations be kept for five (5) years. In addition, the Agency is empowered to inspect and/or require submission of the Section 8(c) records. On August 22, 1983, EPA published (48 FR 38178) the final rule implementing Section 8(c) of TSCA. Full compliance with the Section 8(c) rule has been required since November 21, 1983.

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will transmit a copy of the August 22, 1983, Federal Register (48 FR 38178) notice pertaining to TSCA Section 8(c) to General Motors. In addition, the Chemical Screening Branch will request the General Motors Corporation to provide its rationale as to why the company ultimately decided to report the acute human health effects information to EPA under Section 8(e) of TSCA.

In view of the Agency's general interest in corporate actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the Chemical Screening Branch will request General Motors to describe the actions it has taken to determine the identities and concentrations of the thermal decomposition products of Hypalon Molding Compound in work (and other) areas and to provide the results of such studies to the Agency. In addition, the General Motors Corporation will be requested to describe the actions it has taken, or plans to take, that are designed to reduce and/or eliminate worker and other exposure to the ingredients and thermal decomposition products of Hypalon Molding Compound, and to Hypalon Molding Compound itself.

b) The Chemical Screening Branch will review the reported information to determine if further OTS assessment is warranted at the present time.

c) The Chemical Screening Branch will transmit copies of this status report to NIOSH, OSHA, OW/EPA, OSWER/EPA, OANR/EPA and ORD/EPA. A copy of this report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-1283-0503
Page 1 of 6

DATE: JAN 30 1984

SUBJECT: Status Report* 8EHQ-1283-0503

Approved 2/3/84

Revision Needed ________

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The Dow Chemical Company provided summarized results from several short-term *in vitro* genotoxicity tests on 3-chloro-2-hydroxypropyltrimethylammonium chloride (CAS No. 3327-22-8). According to the submitter, the chemical produced positive responses in an Ames *Salmonella tymphimurium* (bacteria) Mutagenicity Assay, in an Unscheduled DNA Synthesis Assay in cultured rat hepatocytes, and in an Hypoxanthine Guanine Phosphoribosyl Transferase Mutagenicity Assay using cultured Chinese hamster ovary (CHO) cells. Dow reported that 3-chloro-2-hydroxypropyltrimethylammonium chloride is a chemical intermediate having the following two major uses:

> "In the first [use], 3-chloro-2-hydroxypropyltrimethylammonium chloride is reacted with either starch or guar gum to form a wet and dry strength additive in paper. In the second [use], 3-chloro-2-hydroxypropyltrimethylammonium chloride is reacted with hydroxyethyl cellulose to form a component used in shampoos and cosmetics. In both processes, 3-chloro-2-hydroxypropyltrimethylammonium chloride is first converted to the more reactive 2,3-epoxypropyltrimethylammonium chloride [CAS No. 3033-77-0] by raising the pH. The amount of 2,3-epoxypropyltrimethylammonium chloride present in an aqueous solution of 3-chloro-2-hydroxypropyltrimethylammonium chloride is a function of pH. A small amount of 2,3-epoxypropyltrimethylammonium chloride is present in the 3-chloro-2-hydroxypropyltrimethylammonium chloride which Dow manufactures and was present in the compound used in the tests."

According to the submitted information, Dow tested both technical and purified grades of 3-chloro-2-hydroxypropyltrimethylammonium chloride. The technical grade was reported to contain 50.9% 3-chloro-2-hydroxypropyltrimethylammonium chloride and 1.3% to 2.6% 2,3-epoxypropyltrimethylammonium chloride, whereas the purified grade was reported to contain 99% 3-chloro-2-hydroxypropyltrimethylammonium chloride and $\leq$0.1% 2,3-epoxypropyltrimethylammonium chloride.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

In its submission, the Dow Chemical Company also provided copies of two product information letters (dated January 26, 1978 and December 6, 1982) from the Shell International Chemical Company Limited (England) in which Shell International notified its customers (and possibly others) about the results of toxicologic studies that Shell International had conducted or was about to conduct on 2,3-epoxypropyltrimethylammonium chloride. In the 1978 letter, Shell International recounted that previous letters (dated October 30, 1975 and December 1, 1976) had presented information on the primary toxicity of and recommended handling precautions for 2,3-epoxypropyltrimethylammonium chloride. In addition, the 1978 letter reported that 2,3-epoxypropyltrimethylammonium chloride had been found to display mutagenic activity in bacteria and in mammalian cells and reaffirmed the need to follow recommended handling procedures when using the compound. The 1978 letter also reported that chronic mammalian studies of 2,3-epoxypropyltrimethylammonium chloride would be conducted to determine the nature of any long-term effects of exposure to the compound. In its 1982 letter, Shell International reported that the exposure portion of a life-time mouse skin application study of various doses of 2,3-epoxypropyltrimethylammonium chloride had ended and that only the skin had been examined as of the date of the letter. Although the 1982 Shell International letter did not specify what doses were tested, the number of animals tested or whether appropriate controls were used in the chronic mouse skin application study, the letter did present the following preliminary findings from that study:

> "At the top dose, [2,3-epoxypropyltrimethylammonium chloride] produced skin tumors. This dose was set at a level close to the maximum consistent with the long term survival of the animals and the absence of obvious signs of irritation. At the lowest dose there were no skin tumors, while at the intermediate dose the incidence was extremely low."

Considering the nature of the preliminary findings in the life-time mouse skin application study, the 1982 Shell International letter re-emphasized Shell's earlier recommendations to avoid all contact with 2,3-epoxypropyltrimethylammonium chloride. The 1982 Shell International letter also recommended that other companies who had purchased or had received samples of 2,3-epoxypropyltrimethylammonium chloride be contacted to ensure that appropriate handling procedures were being followed. At the end of its 1982 letter, Shell International reported that an evaluation of the final results of the chronic mouse skin application study along with any necessary changes to safe-handling procedures would be communicated in mid-1983.

Dow Chemical Company's Section 8(e) submission did not contain any further correspondence from the Shell International Chemical Company Limited nor did the Dow Chemical Company's submission indicate that Dow had ever received any further correspondence concerning Shell International's life-time mouse skin application study of 2,3-epoxypropyltrimethylammonium chloride.

Submission Evaluation

Dow tested 3-chloro-2-hydroxypropyltrimethylammonium chloride for its ability to induce gene mutation in bacteria (Ames Assay) and in cultured Chinese hamster ovary (CHO) cells. Dow also tested the compound for its ability to induce unscheduled DNA synthesis (UDS) in cultured rat hepatocytes. Although experimental details were not presented in the submission, the submitted data do show that the technical grade of 3-chloro-2-hydroxypropyltrimethylammonium chloride does induce unscheduled DNA synthesis in rat hepatocytes and does induce mutations in Salmonella typhimurium (bacteria) strain TA 1535 (Ames Assay) and cultured CHO cells. The Ames Assay data indicate that the test was performed in the presence and absence of exogenous metabolic activation and that the compound was positive under both conditions. Although the only data that were presented for cultured CHO cells were for an assay that was conducted without metabolic activation, the data were also clearly positive. The provided data also show that a purified sample of 3-chloro-2-hydroxypropyltrimethylammonium chloride induced mutations in Salmonella typhimurium strain TA 1535 when tested both in the presence and absence of exogenous metabolic activation. Although Dow did not submit data on the activity of the purified material in either the cultured CHO or rat hepatocyte assays, there is no reason to believe that the purified material would behave in a different manner in these assays than it does in the Ames Assay.

The submitted Shell International letters contain evidence that 2,3-epoxypropyltrimethylammonium chloride possesses a mutagenic activity both in bacteria and cultured mammalian cells and a dose-dependent oncogenic activity toward mouse skin following chronic skin application; such activities are not necessarily suprising considering that the chemical has a highly reactive epoxide moiety. An initial review of several standard secondary scientific literature sources (e.g., the NIOSH Registry of Toxic Effects of Chemical Substances (RTECS)) and several on-line computerized scientific literature data bases (e.g., TOXLINE) did not, however, reveal any citations indicating that 2,3-epoxypropyltrimethylammonium chloride has been actually shown to display oncogenic activity toward mouse skin following chronic dermal application.

Current Production and Use

A review of the production volume (includes importation volumes) statistics for 3-chloro-2-hydroxypropyltrimethylammonium chloride (CAS No. 3327-22-8), which is listed in the initial TSCA Inventory, has shown that between 1.1 million and 11 million pounds were reported as produced/imported in 1977. A review of the production volume (includes importation volumes) statistics for 2,3-epoxypropyltrimethylammonium chloride (CAS No. 3033-77-0), which is also listed in the TSCA Inventory, has shown that between 210 thousand and 2.1 million pounds of this chemical were reported as produced/imported in 1977. (NOTE: This production range information does not include any production/importation data claimed as confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information which would compromise TSCA Confidential Business Information (CBI). The data submitted for the TSCA Inventory, including the production range information, are subject to the limitations contained in the TSCA Inventory Regulations (40 CFR 710)).

Information submitted by Dow concerning the two major uses of 3-chloro-2-hydroxypropyltrimethylammonium chloride has been incorporated into the Submission Description section of this status report.

Comments/Recommendations

In the cover letter to its submission, Dow stated that it was immediately notifying Dow employees, Dow customers, and other known domestic producers of 3-chloro-2-hydroxypropyltrimethylammonium chloride about the data contained in the company's submission. Dow reported that the company's notification will include a recommendation that "work practices be reviewed in those areas where employees are occupationally exposed to 3-chloro-2-hydroxypropyltrimethylammonium chloride to be sure adequate measures are taken with respect to skin contact and opportunity for ingestion."

EPA believes that the preliminary findings that 2,3-epoxypropyltrimethylammonium chloride produced skin tumors in mice is of the type required for sumbmission under Section 8(e), the substantial risk information reporting provision of the Toxic Substances Control Act (TSCA; 90 Stat. 2029, 15 U.S.C. 2607). It also appears that these preliminary oncogencicity findings should have been submitted to the Agency under Section 8(e) at an earlier date. The basis for the EPA's position is as follows:

> Section 8(e) of TSCA states that "any person who manufactures, processess, or distributes in commerce a chemical substance or mixture and who obtains information which reasonably supports the conclusion that such substance or mixture presents a substantial risk of injury to health or the environment shall immediately inform the [EPA] Administrator of such information unless such person has actual knowledge that the Administrator has been adequately informed of such information."
>
> The preface to Part V of EPA's March 16, 1978 Section 8(e) policy statement ("Statement of Interpretation and Enforcement Policy; Notification of Substantial Risk" 43 FR 11110) states that "a substantial risk of injury to health...is a risk of considerable concern because of (a) the seriousness of the effect...and (b) the fact or probability of its occurrence." With regard to the seriousness of the effect, Part V explains further that that EPA considers the health effects for which substantial risk information must be reported to include "any pattern of effects or evidence which reasonably supports the

conclusion that the chemical substance or mixture can produce cancer...." The information concerning this effect can be obtained directly or inferred from designed studies (e.g., *in vivo* studies as described in Part VI of the 8(e) policy statement). In addition, Part VI explains that "a person is not to delay reporting until he obtains conclusive information that a substantial risk exists, but is to immediately report any evidence which reasonably supports that conclusion." Part VI of the policy document also states that "not only should final results from such studies be reported, but also preliminary results from incomplete studies where appropriate."

With regard to the "fact or probability of its [i.e., the serious effects'] occurrence" criterion, Part V of the policy document explains that certain types of health effects (e.g., cancer, birth defects) are so serious that relatively little weight should be given to a chemical's exposure in determining whether a risk is substantial; the mere fact that an implicated chemical is in commerce would constitute sufficient evidence of exposure.

With regard to the requirement that the EPA Administrator be immediately informed of substantial risk information, Part IV of the 8(e) policy document states that the EPA Administrator is immediately informed "if [substantial risk] information is received by EPA [according to the reporting procedures outlined in Part IX of the policy statement] not later than the 15th working day after the date the [subject] person obtained such information. Part III of the 8(e) policy statement explains that the Agency considers an establishment as having obtained substantial risk information at the time any officer or employee capable of appreciating the significance of such information obtains (i.e., possesses or knows of) such information.

Part VII of EPA's Section 8(e) policy statement explains that the the Agency considers the information about which the EPA Adminstrator has been adequately informed (i.e., information which need not be reported under Section 8(e)) to be that information that has been, for example, published in the scientific literature and abstracted by certain abstract services, or submitted to EPA pursuant to a mandatory reporting requirement under TSCA or other authority administered by EPA.

Based on the preceeding discussion and considering that 1) the preliminary information contained in the December 6, 1982 Shell International Chemical Company letter provides laboratory animal evidence offering reasonable support for the conclusion that 2,3-epoxypropyltrimethylammonium chloride can produce cancer; and 2) the chemical is in commerce thereby indicating the potential for exposure, the Agency believes that the preliminary oncogenicity information contained in the December 6, 1982 letter, when combined with knowledge that the implicated chemical is in commerce, does present reasonable support for a conclusion of a substantial risk of injury to health as defined in EPA's March 16, 1978 Section 8(e) policy statement. Considering that EPA's initial scientific literature review did not reveal any information indicating that 2,3-epoxypropyltrimethylammonium chloride has been shown to produce cancer in mice via skin application, it appears that the preliminary oncogenicity information contained in the December 6, 1982 Shell International Chemical Company's letter submitted by the Dow Chemical Company on December 15, 1983 and received by EPA on December 27, 1983, should have been received by EPA at an earlier date under Section 8(e) of TSCA. In other words, any manufacturer, processor, or distributor of 2,3-epoxypropyltrimethylammonium chloride who obtained preliminary evidence that 2,3-epoxypropyltrimethylammonium chloride can produce cancer in mice following chronic skin application, should have reported such information to EPA under Section 8(e) within 15 working days after obtaining such information.

a) The Chemical Screening Branch (CSB/ECAD/OTS) will request the Dow Chemical Company to submit complete copies of all documents including, but not limited to, preliminary reports, final reports, protocols, data, letters, memoranda, etc. in the possession of the Dow Chemical Company that pertain to the life-time mouse skin application study of 2,3-epoxypropyltrimethylammonium chloride that was cited in the Shell International Chemical Company's December 6, 1982 letter. In addition, the Dow Chemical Company will be requested to provide complete copies of the final reports (including the protocols and data) from all of the in vitro genotoxicity studies on 3-chloro-2-hydroxypropyltrimethylammonium chloride cited in Dow's submission.

   In view of EPA's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the Chemical Screening Branch will request the Dow Chemical Company to describe the actions that the company has taken, or plans to take, that are designed to reduce/eliminate worker and/or other exposures to 2,3-epoxypropyltrimethylammonium chloride. The Chemical Screening Branch will also request the Dow Chemical Company to describe the nature of all studies that the company has conducted, is currently conducting, and/or plans to conduct which are designed to determine the toxicity of 3-chloro-2-hydroxypropyltrimethylammonium chloride and/or 2,3-epoxypropyltrimethylammonium chloride.

b) The Chemical Screening Branch will review the reported information to determine if further OTS assessment of the subject chemicals is warranted at the present time.

c) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OSWER/EPA, OW/EPA, OANR/EPA, ORD/EPA and the Compliance Monitoring Staff (CMS/OPTS/EPA). A copy will also be sent to the TSCA Assistance Office (TAO/OTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0184-0504
Page 1 of 4

DATE: FEB 21 1984

SUBJECT: Status Report* 8EHQ-0184-0504

Approved 2/21

Revision Needed

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The Rio Blanco Oil Shale Company (a general partnership of the Gulf Oil Corporation and the Standard Oil Company (Indiana)) submitted the following summarized findings from a study of a Lurgi light/middle shale oil administered to rats via inhalation at doses of 0, 56, 120, or 490 mg/m^3 for 6 hours per day, 5 days per week for 90 days:

> "In addition to the test animal mortality [57 percent mortality at an aerosol concentration of 490 mg/m^3, with no mortality at 56, 120 mg/m^3 or in the control animal group], a variety of toxicological effects were attributed to test material exposures. These included: dose-related decreases in body weight gain; changes in various organ weights; a variety of clinical observations including ocular and nasal discharges and perianal soiling; decreases in total erythrocytes, leukocytes and platelet counts at the high dose level; elevations in BUN, creatinine, alkaline phosphatase, SGOT and SGPT in the high dose males. The following findings were reported upon histopathological examination and generally increased in frequency and severity as the dose level increased. They included: hyperplasia of the alveolar macrophages; congestion, edema, and atrophy of the bone marrow; severe atrophy of the thymus; atrophy of the lymph nodes; atrophy of the white splenic pulp. Other possibly treatment-related effects included: epithelial necrosis of the proximal convoluted tubules in the kidney; atrophy of the thyroid follicles; acanthosis, hyperkeratosis and focal dermatitis of the skin; atrophy of the testicular epithelium; necrosis of the liver parenchyma. Several neoplasms were observed; none were attributed to test material exposures."

In explaining the rationale for high doses used in the 90-day study, Rio Blanco stated that the study was designed originally as a 30-day pilot study to determine doses which elicit animal toxicity. Rio Blanco also stated that the animal exposures were "excessive relative to observed or anticipated worker exposures."

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Submission Evaluation

According to the submitted information, the liver and kidney damage observed in the male rats was found to increase in both frequency and severity with increasing dose. With regard to the kidney damage, EPA's Office of Toxic Substances has received and evaluated several TSCA Section 8(e) and "For Your Information" submissions in which kidney damage was reported only in male rats exposed to a variety of petroleum fractions. In addition, the liver damage (as evidenced by the observed necrosis and an elevation of serum enzymes) which was reported in this submisssion is not entirely unexpected. It should also be noted that the dermal toxicity (i.e., acanthosis, hyperkeratosis and focal dermatitis) which was observed would not be considered unusual findings if the study involved whole-body exposure to the Lurgi oil.

Although the observed atrophy of the thyroid gland and testicular epithelium are unexpected findings and of biological importance, the submitting company reported that these adverse effects were only "possibly treatment-related."

One of the more striking and potentially life-threatening effects reported in this submission is the apparent dose-dependent damage to hematopoietic/immune functions as evidenced by decreases in total erythrocytes, leukocytes, and platelets; congestion, edema, and atrophy of the bone marrow; severe atrophy of the thymus; and atrophy of the lymph nodes and white splenic pulp. The observed hyperplasia of the pulmonary alveolar macrophages may be a compensatory response to rid the body of the inhaled foreign matter. On balance, however, the provided results indicate that the rats' resistance to infection is profoundly compromised following inhalation of Lurgi light/middle shale oil.

Finally, the Rio Blanco Oil Shale company reported that several neoplasms had been observed but not attributed to exposure to the test material. In order for the Agency to evaluate better the neoplastic and other toxicologic findings reported in this submission, a full copy of the final report, including experimental protocols and data, should be requested from the Rio Blanco Oil Shale Company.

Current Production and Use

In general, crude shale oils are obtained from oil shale via a destructive distillation process followed by hydrotreating. The Lurgi-Ruhrgas process involves indirect heating whereby heat is transferred by mixing hot retorted shale with oil shale resulting in high oil yields and high quality product gas. Although the Rio Blanco Oil Shale Company did not provide any information concerning the current or planned production volumes of the Lurgi light/middle shale oil, the company did report that its Lurgi process development operations are located in a pilot plant at a Gulf Oil Corporation facility.

A review of the production range (includes importation volumes) statistics for shale oils having the CAS No. 68308-34-9 (which is listed in the initial TSCA Inventory) has shown that between 11 million and 61 million pounds were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed as confidential by person(s) reporting for the TSCA Inventory, nor does it include any information that would compromise Confidential Business Information. The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

Comments/Recommendations

In its submission, Rio Blanco stated that the company "has been conducting a toxicity testing program in conjunction with the development of methods for shale oil extraction" and that the toxicity testing program included studies of oils derived from shale via the Lurgi retorting technology. Rio Blanco also stated that "industrial hygiene monitoring at the pilot plant has shown minimal organic aerosol exposure to workers, below OSHA standards and usually below detection limits" and that "the industrial hygiene monitoring and work practices being employed at the pilot plant are adequate to prevent health risk to workers."

EPA's Office of Toxic Substances has received and evaluated many TSCA Section 8(e) and/or "For Your Information" (FYI) submissions containing toxicologic and/or exposure information on a variety of coal-, shale- (including Lurgi), and petroleum-derived oil products, process intermediates, and/or waste materials.

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will request the Rio Blanco Oil Shale Company to provide a complete copy of the final report, including protocol(s) and data, from the 90-day rat inhalation study of Lurgi light/middle shale oil which was cited in the company's submission. Rio Blanco will also be requested to submit the actual results of the industrial hygiene monitoring study conducted at the Lurgi process pilot plant.

In view of the Agency's general interest in corporate actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, Rio Blanco will also be requested to describe the nature of studies that the company has conducted, is conducting, or plans to conduct, that are designed to define the toxicity of and/or exposure to Lurgi light/middle shale oil and/or other oil shale-derived materials.

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of Lurgi light/middle shale oil at the present time.

c) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, CPSC, NTP, DOE, OW/EPA, OSWER/EPA, OANR/EPA, ORD/EPA and to the OTS "Synfuels Workgroup." A copy of this status report will also be provided to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0284-0505
Page 1 of 3

DATE: MAR 15 1984

SUBJECT: Status Report* 8EHQ-0284-0505

Approved 3/16/84

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section

Revision DEC - 5 1984

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS

Submission Description [See NOTE on Page 3 of this Status Report]

On behalf of the Amoco Oil Company, the Standard Oil Company (Indiana) submitted the following summarized preliminary findings from a three week rat dermal toxicity study of a solvent-refined heavy paraffinic distillate (CAS No. 64741-88-4) that had been processed further by dewaxing:

> "The test animals [(rats)] were divided into two groups, each consisting of 10 males and 10 females. One group was treated with 2.0 ml/kg of base oil by application on the skin for 15 consecutive weekdays. The rats in the sham control group did not receive the test material but were otherwise handled exactly like the treated rats. There were no treatment related lesions observed in the treated or sham control group upon gross observation. However, microscopic examination did indicate testicular lesions of all male rats at the 2.0 ml/kg dose level. The testicular lesions were characterized by diffuse hypoplasia and degeneration of germinal cells in the seminiferous tubules."

The submitter stated that the single dose level used in the study did not permit establishment of a dose-response relationship and that the study was not designed to examine the reversibility of the observed effects.

Submission Evaluation [See NOTE on Page 3 of this Status Report]

According to the provided summarized information, the testicular lesions (characterized by "diffuse hypoplasia and degeneration of the germinal cells in the seminiferous tubules") were observed microscopically in all (10/10) male rats following exposure to a dewaxed solvent-refined heavy paraffinic petroleum distillate applied to the skin at a dose of 2.0 ml/kg for 15 consecutive weekdays. Although the 100% incidence of testicular lesions in the treated male rats indicates that the observed adverse effects on the testes are real, further evaluation of the reported (and other?) findings should be possible upon EPA's receipt of a complete copy of the final report which should include the study protocol and data.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Current Production and Use

The test material was described by the submitter as a "solvent-refined heavy paraffinic distillate (CAS No. 64741-88-4) which is further processed by dewaxing." The submitter stated also that although there are other solvents that can be used in solvent-refining, the solvent used in this case was N-methylpyrrolidone.

According to Volume I of the TSCA Chemical Substances Inventory, solvent-refined heavy paraffinic distillates are defined as "a complex combination of hydrocarbons obtained as the raffinate from a solvent extraction process [and] consists predominantly of saturated hydrocarbons having carbon numbers predominantly in the range of C20 through C50 and produces a finished oil with a viscosity of at least 100 SUS at 100°F (19cSt at 40°C)."

A review of the production range (includes importation volumes) statistics for solvent-refined heavy paraffinic distillate (CAS No. 64741-88-4), which is listed in the initial TSCA Inventory, has shown that in excess of 9.5 billion pounds were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed as confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information that would compromise TSCA Confidential Business Information. The data submitted for the TSCA Inventory, including the production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

Comments/Recommendations

The Standard Oil Company (Indiana) stated that when the subject 3-week dermal toxicity study has been completed, a copy of the final report will be forwarded to EPA.

EPA's Office of Toxic Substances has received and evaluated many TSCA Section 8(e) and "For Your Information" (FYI) submissions containing toxicologic and/or exposure information on a variety of petroleum oils, process streams and/or wastes.

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will request the Standard Oil Company (Indiana) to ensure that the Agency recieves, upon completion, a full copy of the final report including protocol(s) and data from the 3-week rat dermal toxicity study of the dewaxed solvent-refined heavy paraffinic distillate. In view of EPA's general interest in corporate actions that are taken on a voluntary basis in response to chemical toxicity and/or exposure information, the submitter will also be requested to describe the nature of all studies that the Standard Oil Company (Indiana) and the Amoco Oil Company have conducted, are conducting, or plan to conduct to define the toxicity of and/or exposure to dewaxed solvent-refined heavy paraffinic distillate.

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of dewaxed solvent-refined heavy paraffinic distillate at the present time.

c) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, CPSC, NTP, DOE, OW/EPA, OSWER/EPA, OANR/EPA, and ORD/EPA. A copy of this status report will also be transmitted to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

NOTE: In follow-up submissions dated October 10, 1984 and November 9, 1984, the Standard Oil Company (Indiana) provided complete copies of the final reports from the subject 3-week dermal application study as well as from a repeated study. In summary, the submitted information shows that the adverse testicular effects reported in the initial TSCA Section 8(e) notice were actually artifacts that resulted from improper tissue sectioning of testes from the treated animals. In addition, data from the repeated 3-week study show that there were no adverse morphological effects in the testes of rats exposed dermally to dewaxed solvent-refined heavy paraffinic distillate.

The Chemical Screening Branch will transmit copies of this updated status report to the submitting company and to all EPA Offices and Federal Agencies that are listed in c) above.

12/5/84

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0384-0506 S
Page 1 of 3

DATE: MAR 27 1984

SUBJECT: Status Report* 8EHQ-0384-0506 S

Approved 4/2/84

Revision Needed ________

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The submitting company (company name claimed as TSCA Confidential Business Information (TSCA CBI)) provided summarized results from a battery of *in vitro* and *in vivo* genotoxicity studies of 1,3,5-triacryloylhexahydro-s-triazine (CAS No. 959-52-4). According to the submitter, the results of the performed studies showed that:

> "1,3,5-triacryloylhexahydro-s-triazine did not produce activity, *in vitro*, consistent with that of a chemical mutagen in a forward point mutation assay in CHO [Chinese Hamster Ovary] cells, in a sister chromatid exchange test in CHO cells, or in a test for the unscheduled synthesis of DNA. The presence of chromosomal aberrations in the CHO cells used in the sister chromatid exhcange test was confirmed, in a concentration related manner, as an *in vitro* clastogenic effect by the conduct of a definitive cytogenetic test in cultured CHO cells. Additional confirmation of the clastogenic potential of the triazine chemical was demonstrated, *in vivo*, by a micronucleus test in mice. These findings indicate that 1,3,5-triacryloylhexahydro-s-triazine is a clastogenic material, but devoid of mutagenic activity."

Submission Evaluation

According to the submitted information, 1,3,5-triacryloylhexahydro-s-triazine was tested in a battery of assays which included tests for gene mutation (HPRT locus) in cultured Chinese Hamster Ovary (CHO) cells, Sister Chromatid Exchange (SCE) formation in cultured CHO cells, Unscheduled DNA Synthesis (UDS) in isolated rat hepatocytes, chromosomal aberrations in cultured CHO cells, and micronucleus formation in peripheral blood of Swiss-Webster mice. These assays were conducted in three stages with the *in vitro* CHO cell gene mutation, SCE, and UDS assays being conducted *first*. Although the reported findings from the first stage assays did not provide any evidence that the chemical caused gene mutation, SCE formation, or UDS, the cultured CHO cells used in the SCE assay were reported to have shown an abnormally high frequency of chromosomal aberrations. In order to confirm this finding, a chromosomal aberration assay in cultured CHO cells was performed. According to the submitted information, the results of this assay showed that chromosomal aberrations were induced in a dose-related manner (beginning with the lowest dose) both with and without exogenous metabolic activation. Finally, the subject chemical was tested for its ability to induce micronuclei in the peripheral blood of male and female Swiss-Webster mice following intraperitoneal injection. The provided results indicate that micronuclei were induced in a dose-related manner in both sexes.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Although the submitted findings do not provide any evidence that 1,3,5-triacryloylhexahydro-s-triazine is a mutagen, the chemical does appear to possess clastogenic activity as evidenced by the induction of chromosomal aberrations in vitro and micronuclei in the peripheral blood of treated animals. Complete copies of the final reports (including test protocols and data) from all of the tests cited in this submission would be needed to evaluate better the findings reported for this chemical.

Current Production and Use

A review of the production range (includes importation volumes) statistics for 1,3,5-triacryloylhexahydro-s-triazine (CAS No. 959-52-4), which is listed in the initial TSCA Inventory, has shown that no 1977 production/importation was reported or that all of the production range data reported were claimed as confidential by the manufacturer(s) and/or importer(s) and cannot be disclosed (Section 14(a) of TSCA, U.S.C. 2613 (a)). The data submitted for the Inventory, including production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

The submitting company did not provide any information concerning the use(s) of 1,3,5-triacryloylhexahydro-s-triazine nor was any information on the use(s) of this chemical located in the secondary literature sources consulted by EPA.

Comments/Recommendations

The submitter stated that because the company has "recognized from the outset that the material had the potential of biological activity, [the company] initiated and continues to take measures to protect employees working in research and development from the cytotoxic effects of 1,3,5-triacryloylhexahydro-s-triazine by various safety handling procedures [including] avoidance of skin contact by the use of protective body and hand clothing, and the [use] of respiratory protective equipment. The submitter also stated that "the only U.S. supplier and the only foreign manufacturer known to the submitter" were being notified about the reported information. Finally, the submitter stated that the final reports of the studies cited in the submission would be transmitted to EPA when the reports are completed.

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will request the submitting company to ensure that the Agency receives complete copies of the final reports (including protocols and data) from all of the genotoxicity studies cited in the company's submission on 1,3,5-triacryloylhexahydro-s-triazine.

In view of the Agency's general interest in corporate actions which are taken on a voluntary basis in response to chemical toxicity and/or exposure information, the Chemical Screening Branch will request the submitting company to describe all other studies that the company has conducted, is now conducting, or is planning to conduct that define the toxicity of and/or exposure to 1,3,5-triacryloylhexahydro-s-triazine.

b) The Chemical Screening Branch will review the reported information to determine if further OTS assessment of 1,3,5-triacryloylhexahydro-s-triazine is warranted at the present time.

c) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA and ORD/EPA. A copy of this status report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0384-0507
Page 1 of 3

DATE: APR - 5 1984

SUBJECT: Status Report* 8EHQ-0384-0507

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Approved 4/6/84

Revision Needed ____________

Submission Description

The Gulf Oil Products Company submitted summarized findings from a 13-week dermal toxicity study of Gulf Process 65 Oil (CAS No. 64742-11-6), Gulf 100 Texas Distillate (Cas No. 64741-53-3) and Gulf 100 Texas Oil (CAS No. 64742-52-5). According to the submitted information,

> "Gulf Process 65 Oil and Gulf 100 Texas Distillate were each painted on the backs of C3H mice, 50 males and 50 females per dose level, at two dose levels (50 µl undiluted and 50 µl diluted 50% w/v mineral oil), 3 times/week for 13 weeks. At the end of that time, all treated and control animals were necropsied and subjected to gross and microscopic pathological examination. The application of Process 65 Oil resulted in the appearance of one squamous cell carcinoma and one benign papilloma. The application of 100 Texas Distillate produced one squamous cell carcinoma and two benign papillomas.... The application [same protocol] of 100 Texas Oil did not result in the appearance of any neoplasms. However, it did produce histological changes in the skin, including mild to moderate levels of epidermal acanthosis and hyperkeratosis in both sexes."

Submission Evaluation

The submitted results from the 13 week dermal toxicity study indicate that Gulf Process 65 Oil and Gulf 100 Texas Distillate possess oncogenic activity toward mouse skin. A more complete evaluation of the reported findings should be possible upon EPA's receipt of the final report which should include all protocols and test data.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Current Production and Use

Volume I of the TSCA Chemical Substances Inventory, defines the test materials by CAS Number as follows:

> CAS No. 64741-53-3 (Gulf 100 Texas Distillate): "...a complex combination of hydrocarbons produced by vacuum distillation of the residuum from atmospheric distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly in the range of C20-C50 and produces a finished oil with a viscosity of at least 100 SUS at 100°F (19cSt at 40°C). It contains relatively few normal paraffins."
>
> CAS No. 64742-11-6 (Gulf Process 65 Oil): "...a complex combination of hydrocarbons obtained as the extract from a solvent extraction process. It consists predominantly of aromatic hydrocarbons having carbon numbers predominantly in the range of C20-C50. This stream is likely to contain 5 wt% or more of 4- to 6- membered condensed ring aromatic hydrocarbons."
>
> CAS No. 64742-52-5 (Gulf 100 Texas Oil): "...a complex combination of hydrocarbons obtained by treating a petroleum fraction with hydrogen in the presence of a catalyst. It consists of hydrocarbons having carbon numbers predominantly in the range of C20-C50 and produces a finished oil of at least 100 SUS at 100°F (19cSt at 40°C). It contains relatively few normal paraffins."

A review of the production range (includes importation volumes) statistics for the subject test materials, which are listed in the Initial TSCA Inventory, shows that in excess of 6.6 billion pounds, between 1.2-2.9 billion pounds, and in excess of 2.1 billion pounds for CAS No's 64741-53-3, 64742-11-6 and 64742-52-5, respectively, were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed as confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information that would compromise TSCA Confidential Business Information. The data submitted for the TSCA Inventory, including the production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

Comments/Recommendations

The Gulf Oil Products Company stated that when the final report from the subject 13-week dermal toxicity study is available, a copy will be forwarded to EPA. The company also stated that it is reviewing the current "handling procedures, labeling practices and Material Safety Data Sheets to determine if any changes are needed to assure safe handling for Gulf's employees, contractors or customers."

EPA's Office of Toxic Substances (OTS) has reviewed and evaluated previously submitted toxicologic information on Gulf Process 65 Oil and Gulf 100 Texas Oil (8EHQ-0281-0385 et seq.) as well as many other TSCA Section 8(e) and "For Your Information" (FYI) submissions containing toxicologic and/or exposure information on a variety of petroleum oils, process streams and/or wastes.

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will request the Gulf Oil Products Company to ensure that the Agency receives, when available, a full copy of the final report (including protocol(s) and data) from the 13-week mouse dermal toxicity study on Gulf Process 65 Oil, Gulf 100 Texas Distillate and Gulf 100 Texas Oil.

   In view of EPA's general interest in corporate actions that are taken on a voluntary basis in response to chemical toxicity and/or exposure information, the Gulf Oil Products Company will also be requested to describe the nature of all studies that it has conducted (exclusive of the previously submitted toxicologic information), is conducting or plans to conduct to further define the toxicity of and/or exposure to the test materials.

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of Gulf Process 65 Oil, Gulf 100 Texas Distillate and/or Gulf 100 Texas Oil at the present time.

c) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, CPSC, NTP, DOE, OW/EPA, OSWER/EPA, OANR/EPA and ORD/EPA. A copy of this status report will also be transmitted to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0384-0508 P
Page 1 of 3

DATE: APR 23 1984

SUBJECT: Status Report* 8EHQ-0384-0508 P

Approved 4/24

Revision Needed ____

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

Racon Inc. reported that on January 24, 1984, five Racon workers were exposed accidentally to a number of chemicals released due to an overpressurization in a shutdown reactor. According to the submitted information, hydrochloric acid, hydrofluoric acid, refrigerants (unspecified), and antimony pentachloride were in the reactor at the time of the incident. Racon stated that the five exposed workers experienced acute reactions (i.e., headache; eye, nose and throat irritation; and some chest and arm pains) commonly known to occur after exposure to such chemicals. Racon also stated that although the five employees did not require hospitalization and all symptoms have since disappeared, four of the exposed workers did go to physicians and four of the exposed workers prepared complaint reports. Racon reported that it had decided to place the four reports in the company's TSCA Section 8(c) file and to submit two of those reports under Section 8(e)

Submission Evaluation

Racon's decision to submit the two Section 8(c) reports under 8(e) appears to have been based mainly on conflicting medical opinions as to the cause(s) of "internal nose blisters" noted in one report and a "sharp pain in the abdomen followed by swelling" noted in the other report. Although it is not possible to determine if the abdominal pain and subsequent swelling experienced by one of the workers was chemical-related, all of the other signs and symptoms are of the type that can occur following exposure to potent irritants such as hydrochloric and hydrofluoric acid. In general, all of the exposed workers appear to have recovered in a relatively short period of time.

Current Production and Use

Due to the nature of this submission, production/use information on the subject chemicals will not appear in this status report.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Comments/Recommendations

It is the Agency's position that the acute human toxic effects information, as presented in Racon's notice, did not need to be submitted under Section 8(e), the substantial risk information reporting provision of the Toxic Substances Control Act (TSCA). The basis for EPA's position with regard to the Section 8(e)-applicability of the reported information is as follows:

> According the Part V of the Agency's March 16, 1978, TSCA Section 8(e) policy statement ("Statement of Interpretation and Enforcement Policy; Notification of Substantial Risk" 43 FR 11110), a "substantial risk of injury to health...is a risk of considerable concern because of (a) the seriousness of the effect...and (b) the fact or probability of its occurrence." With regard to the seriousness of the effect, EPA considers the human health effects for which substantial risk information must be reported to include "any instance of cancer, birth defects, mutagenicity, death or serious or prolonged incapacitation, including the loss of or inability to use a normal bodily function with a consequent relatively serious impairment of normal activities if one (or a few) chemical(s) is strongly implicated." In addition, Part VI(2) of the 8(e) policy document states that it is possible that effects less serious than those described above may be preliminary manifestations of those more serious effects and together with another triggering piece of information, constitute Section 8(e)-reportable information.

In view of the above discussion and considering that the acute human health effects reported in Racon's submission do not appear to be serious or to have resulted in prolonged incapacitation or serious impairment or loss of normal bodily functions, the Agency believes that the information did not need to be reported under Section 8(e). It must be emphasized, however, that the Agency's position with regard to 8(e)-reportability is based solely on the submitted information and not on other pertinent information that may have been available to and considered by Racon in deciding to report the information under Section 8(e).

It is also important to note that although EPA does not believe that the human health effects information, as presented in the Racon submission, warranted reporting under TSCA Section 8(e), the Agency does believe that the employees' reports may be of the type required to be maintained by the company under Section 8(c), a major recordkeeping provision of TSCA. On August 22, 1983, EPA published (48 FR 38178) a final Section 8(c) rule that required full compliance with 8(c) of November 21, 1983. In general, the Section 8(c) rule requires chemical manufacturers and certain processors to maintain records of significant adverse reactions to health or the environment alleged to have been caused by chemical substances or mixtures. The Section 8(c) rule also requires that allegations involving significant adverse reactions in employees be kept for 30 years and that all other allegations be kept for 5 years. The Agency is empowered to both inspect and require submission of TSCA Section 8(c) records. It should be noted, however, that there are no automatic Section 8(c) record reporting requirements in place at the present time.

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will ask Racon Inc. to provide the company's rationale as to why the acute human health effects information was reported to EPA under Section 8(e), the substantial risk information reporting provision of TSCA.

b) The Chemical Screening Branch will review the reported information to determine if further OTS assessment is warranted at the present time.

c) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, OW/EPA, OSWER/EPA, OANR/EPA and ORD/EPA. A copy of this report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

Page 1 of 7

DATE: MAR 13 1984

SUBJECT: Status Report* 8EHQ-1083-0509 and
8EHQ-0184-0509 Followup

Approved 3/24/84

Revision
Needed ______

FROM: Frank D. Kover
Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS

TO: Joseph J. Merenda, Director
Existing Chemical Assessment Division/OTS

Submission Description

In response to an informal EPA request for information on diethyl sulfate (CAS No. 64-67-5), the Union Carbide Corporation provided a final report from each of the following Union Carbide-sponsored studies: 1) "Evaluation of the Dermal Carcinogenic Potential of Diethyl Sulfate" (report dated July 26, 1979) and 2) "Diethyl Sulfate - In Vitro Mutagenesis Studies: 3-Test Battery" (report dated September 17, 1980). (In view of the fact that the Union Carbide Corporation sent these reports to the Agency on a "For Your Information" (or FYI) basis, the following Document Control Number was assigned to the information: FYI-OTS-1083-0271).

The following findings were presented in the July 26, 1979 report of the Union Carbide Corporation's dermal carcinogenicity study of diethyl sulfate:

> "A group of 40 C3H/HeJ male mice was painted 3 times per week for their lifespan on the skin of the back, clipped free of fur, with undiluted diethyl sulfate at an average dose of 0.0074 grams diethyl sulfate/mouse/application. A negative control group of 40 C3H/HeJ male mice received skin paintings of acetone three times per week at an average dose of 0.0126 grams acetone/mouse/application and a positive control group of 40 C3H/HeJ male mice received skin paintings of methylcholanthrene as a 0.2% dilution in benzene three times per week at an average dose of 0.033 milligrams/mouse/application. Both diethyl sulfate and methylcholanthrene showed dermal carcinogenic activity in mice. The median latent periods, which are measures of relative potency, were approximately 16 months for diethyl sulfate as compared to 4 to 5 months for methylcholanthrene. The tumor and cancer indices for the diethyl sulfate group were both 87.5 as compared to 100 and 94.4, respectively, for the group painted with methylcholanthrene. No skin tumors were observed in the mice painted with acetone."

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

According to Union Carbide, the company selected diethyl sulfate for genotoxicity testing because the chemical was positive in the mouse dermal carcinogenesis assay. The following information was contained in the September 27, 1980 report of the Union Carbide Corporation's genotoxicity studies of diethyl sulfate:

> "Diethyl sulfate was evaluated for potential mutagenic activity with a battery of three in vitro tests, which were: the Chinese Hamster Ovary (CHO) Mutation test, the Sister Chromatid Exchange (SCE) test and an assay for [the] induction of Unscheduled DNA Synthesis (UDS) in rat liver cells. The pattern of positive responses obtained in the 3-test battery of mutagenicity assays indicated that diethyl sulfate produced a significant mutagenic effect typical of identified chemical mutagens and appeared to possess significant mutagenic potential in all three of the in vitro tests performed."

In the performed Chinese Hamster Ovary Mutation assay, all test concentrations of diethyl sulfate were reported to have produced a statistically significant and dose-related increase in mutation frequency both with and without S9 metabolic activation. In the Sister Chromatid Exchange assay, diethyl sulfate was reported to have produced a highly statistically significant and dose-related increase in SCE frequency at the low and mid-dose levels without S9 activation and the high dose was reported to be cytotoxic. The SCE report further stated that "the sample of diethyl sulfate was classified as a positive mutagenic agent by direct action and testing with an S9 activation system was not performed." In the performed Unscheduled DNA Synthesis assay, diethyl sulfate was reported to have induced statistically significant increases in UDS detected both with nuclei and DNA. According to the UDS report, "diethyl sulfate was classified as an active mutagenic agent in the induction of UDS in the present test with the hepatocyte test system."

In addition to the previously described toxicologic reports, the Union Carbide Corporation provided to EPA a copy of the company's product literature sheet and a May 1, 1981 Material Safety Data Sheet (MSDS) on diethyl sulfate. The MSDS states that "diethyl sulfate has been shown to be...carcinogenic in chronic laboratory animal experiments."

Following EPA's initial review of the provided genotoxicity and carcinogenicity data (see the Submission Evaluation section of this status report), the Union Carbide Corporation was informed (EPA letter dated December 12, 1983) that the Agency believed that Union Carbide's observation that diethyl sulfate produced benign/malignant skin tumors in mice following repeated dermal application was new "substantial risk" information which should have been submitted at an earlier date to EPA under Section 8(e), the substantial risk information reporting provision of the Toxic Substances Control Act (TSCA). Union Carbide was requested to provide its rationale as to why the subject oncogenicity findings had not been submitted in a timely manner under Section 8(e).

In a letter dated January 25, 1984 (FYI-OTS-0284-0271 Followup), the Union Carbide Corporation responded to EPA's question about the Section 8(e)-reportability of a positive carcinogenic effect in a species (mouse) and via a route of exposure (skin painting) for which such an effect has not been previously reported. In addition to citing a number of scientific publications relating to the oncogenic activity (and other toxic effects) of diethyl sulfate (and dimethyl sulfate), Union Carbide provided a description of the company's activities (beginning in 1975) that were designed to further define the toxicity of diethyl sulfate and to reduce and/or eliminate worker exposure to the chemical.

According to Union Carbide, the chronic mouse skin application study of diethyl sulfate was started in 1976 and was part of a Union Carbide product safety initiative for the chemical. Union Carbide stated that on September 16, 1977, the director of the study reported to the company's toxicology advisory group that "some mice had developed skin tumors and cancers." Union Carbide also stated that the study director's September 16, 1977 report was made via an established "system for early notification to the toxicology group of any adverse effects as they developed during the course of such studies."

With regard to Union Carbide's rationale for not reporting the company's findings that diethyl sulfate produced skin cancer in mice following chronic dermal application, Union Carbide provided the following information:

> "The informal group who reviewed the preliminary data from the mouse study concluded that the information was not subject to reporting since it corroborated the fact that diethyl sulfate was established as an animal carcinogen in rat studies as stated in [the 1977 NIOSH Registry of Toxic Effects of Chemical Substances (RTECS)]. [The group's] judgment was reinforced by the fact that diethyl sulfate was a known mutagen and a structural analogue of dimethyl sulfate, a known carcinogen."

With regard to EPA's belief that Union Carbide's finding of skin cancer in mice following chronic dermal application had not been previously reported for diethyl sulfate, Union Carbide stated that the Agency was correct. Union Carbide also stated, however, that the Agency's March 16, 1978 Section 8(e) policy statement ("Statement of Interpretation and Enforcement Policy; Notification of Substantial Risk" 43 FR 11110) "does not indicate that a carcinogenic effect in an animal study will not be considered by EPA to be corroborative of a previously reported carcinogenic effect if it occurs in a different species and by a different route of exposure."

The Union Carbide Corporation's rationale for not reporting the subject oncogenicity findings will be addressed by the Agency in the Comments/Recommendations section of this status report.

Submission Evaluation

Like other alkylsulfates, diethyl sulfate appears to be a typical alkylating agent. The carcinogenicity (and mutagenicity) of its homolog, dimethyl sulfate, is well known. Dimethyl sulfate has been shown to be carcinogenic in rats following inhalation or subcutaneous administration, but negative in mice following dermal application or intravenous administration. Diethyl sulfate has been shown to be carcinogenic in rats following subcutaneous injection or via transplacental exposure. The test results provided by Union Carbide clearly demonstrate that diethyl sulfate is also a moderate/potent carcinogen toward the skin of C3H/HeJ male mice following dermal application (when evaluated against 3-methylcholanthrene as a positive control). The positive results from the performed 3-test genotoxicity battery are consistent with the diethyl sulfate carcinogenicity bioassay findings and previously reported genotoxicity test results for this chemical substance.

Although Union Carbide's bioassay does demonstrate the dermal carcinogenicity of diethyl sulfate in mice, the inbred mouse strain used in the study may not have been the best choice to assess the full carcinogenic potential of diethyl sulfate in terms of multiplicity of tissue targets affected. Inbred mouse strains may possess an unusual sensitivity or resistance to the development of any given tumor type. Indeed, the C3H/HeJ mice in the acetone (negative control) group displayed a high spontaneous incidence of hepatic tumors. It may have been a better choice to use random-bred Swiss mice which are known to have a generally low incidence of spontaneous neoplasms.

Production and Use

A review of the production range (including importation volumes) statistics for diethyl sulfate (CAS No. 64-67-5), which is listed in the initial TSCA Inventory, has shown that between 1.25 million and 12.5 million pounds were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed to be confidential by those person(s) reporting for the TSCA Inventory, nor does it include any information that would compromise TSCA Confidential Business Information. All of the data submitted for the TSCA Inventory, including the production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

According to secondary literature sources and product information provided by the Union Carbide Corporation, diethyl sulfate can be used as an ethylating agent in the manufacture of aliphatic and aromatic ethers, amines, amides, and esters for dyestuff and pharmaceutical synthesis, in the manufacture of quaternary textile finishing compounds, as an accelerator in the sulfation of ethylene and in some sulfonations. It can be produced by absorbing ethylene in concentrated sulfuric acid or by the action of fuming sulfuric acid on ethyl ether or ethyl alcohol. Diethyl sulfate is also produced as an intermediate in one method for the production of ethyl alcohol from ethylene.

Comments/Recommendations

EPA's position is unchanged with regard to the TSCA Section 8(e)-applicability/reportability of the Union Carbide Corporation's oncogenicity findings in mouse skin following chronic dermal application of diethyl sulfate. EPA believes that Union Carbide's findings do not corroborate those already documented for diethyl sulfate and therefore should have been submitted to EPA in a timely manner pursuant to Section 8(e) of TSCA.

It is EPA's experience that chemical companies subject to Section 8(e) consider a number of factors (including those listed below) in determining whether obtained information may warrant reporting to EPA under Section 8(e) of TSCA:

1) species (and strain of species) tested;
2) nature (including severity) of the observed effect(s);
3) time to onset of the observed effect(s);
4) target organ(s);
5) route of exposure/administration; and
6) dose(s) administered

It should be noted that new information relating to such factors does play an extremely vital role in 1) assessing, and in some cases, re-assessing the degree of risk of injury to health or environment posed by exposure to a chemical substance or mixture, and 2) determining the most appropriate course(s) of action for reducing or eliminating such risk. For example, a risk assessment which is based on a reported finding that chemical X can produce injection-site sarcomas in rats could be changed in a significant way by new information which indicates that chemical X can produce lung or other tumors via inhalation in rats. Such a change in the risk assessment could lead in many cases to a change in the course of the action(s) needed to reduce risk. It should be evident, therefore, that an observation that chemical X produces lung or other tumors via inhalation should not be viewed as simply corroborating a previously reported and/or well known observation that the chemical produces injection-site sarcomas following subcutaneous injection.

Many chemical manufacturers, processors, and distributors have correctly recognized that in order for new health effects information to be corroborative, the information must verify or confirm previously reported and/or published information that the subject chemical substance or mixture when administered at a specific dose by a specific route produced a specific toxic effect (e.g., squamous cell carcinoma) in a specific target organ (e.g., skin) in a specific species or strain of species. This interpretation is supported by the fact that many companies who have submitted information under Section 8(e) have reported that their decision to submit was based on the fact that a difference observed in as few as one of the previously listed factors had caused the obtained information to become sufficiently different from that which was previously known for the tested chemical substance or mixture. EPA continues to believe that the interpretation is correct and consistent with the legislative intent of TSCA and the legislative intent and language of the Section 8(e) provision itself. EPA also continues to believe that the preponderant industry interpretation is consistent with the Agency's well publicized concern about cancer (as well as other serious health effects) and with the intent and language of the Agency's Section 8(e) policy statement with regard to the timely reporting of such serious health effects information.

The preface to Part V of EPA's March 16, 1978, TSCA Section 8(e) policy statement (i.e., "Statement of Intrepretation and Enforcement Policy; Notification of Substantial Risk" 43 FR 11110) states the Agency's belief that a "substantial risk of injury to health or the environment is a risk of considerable concern because of (a) the seriousness of the effect...and (b) the fact or probability of its occurrence." With regard to the seriousness of the effect, Part V explains that EPA considers the health effects for which substantial risk information must be reported to include "any pattern of effects or evidence which reasonably supports the conclusion that the chemical substance or mixture can produce cancer, mutation, birth defects or toxic effects resulting in death or serious or prolonged incapacitation. Information concerning these effects can be obtained directly or inferred from designed studies (e.g., *in vivo* experiments and tests as described in Part VI of the policy statement). With regard to the "fact or probability of its occurrence" criterion, Part V explains that certain types of health effects (e.g., cancer) are so serious that relatively little weight should be given to the chemical's exposure in determining whether a risk is substantial; the mere fact that an implicated chemical or mixture is in commerce would constitute sufficient evidence of exposure.

In the case of the information provided in FYI-OTS-1083-0271, the Union Carbide Corporation found that diethyl sulfate can produce skin cancers in mice after repeated dermal application, a finding which the company has acknowledged was not previously known for diethyl sulfate. For the purposes of Section 8(e)-reporting, EPA does not believe that this finding corroborates information that had been previously reported to EPA or published in the available scientific literature. Therefore, EPA has determined that Union Carbide should have reported its mouse skin cancer findings for diethyl sulfate to EPA in a timely manner under Section 8(e) of the Toxic Substances Control Act.

The Risk Management Branch (RMB/ECAD/OTS/OPTS) has been assessing available toxicity and exposure information on diethyl sulfate in order to determine the need for and scope of a formal (or other) EPA response designed to reduce potential risks posed by exposure to this chemical. In addition, it should be noted that diethyl sulfate was listed in EPA's June 22, 1982 TSCA final Section 8(a) chemical exposure information-reporting rule (47 FR 26992).

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will inform the Union Carbide Corporation of EPA's determination concerning the Section 8(e)-reportability of the company's observation that diethyl sulfate can produce skin cancers in mice following repeated dermal application. In light of this EPA determination, the Chemical Screening Branch will deliver FYI-OTS-1083-0271 and FYI-OTS-0284-0271 Followup Response to the Document Control Office (DCO/IMD/OTS/OPTS) for appropriate handling/filing under Section 8(e) of the Toxic Substances Control Act.

b) The Chemical Screening Branch will send a copy of this status report to OSHA, NIOSH, CPSC, FDA, NTP, OANR/EPA, ORD/EPA, OW/EPA, OSWER/EPA, RMB/ECAD/OTS/OPTS, and the Compliance Monitoring Staff (CMS/OPTS). A copy of this report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0484-0510
Page 1 of 3

DATE: APR 16 1984

SUBJECT: Status Report* 8EHQ-0484-0510

Approved 4/16/84

Revision Needed ______

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The IBM Corporation provided summarized results from several in vitro genotoxicity and in vivo acute toxicity studies of 2,3,4-trihydroxybenzophenone (THBP; CAS No. 1143-72-2). According to IBM, THBP was found to induce Sister Chromatid Exchanges (SCEs) in cultured Chinese Hamster Ovary (CHO) cells in the presence and absence of exogenous metabolic activation and found to produce chromosomal aberrations in cultured CHO cells in the presence but not in the absence of exogenous metabolic activation. IBM also reported that THBP had been found to be non-mutagenic in the presence and absence of metabolic activation in a previously conducted Ames/Salmonella typhimurium (bacteria) assay. With regard to the negative results of the chromosomal aberration assay that was conducted in the absence of metabolic activation, the submitter stated that the validity of these results was in question and expressed the company's opinion that positive results might be obtained using higher doses of THBP.

In addition to the submitted in vitro genotoxicity information, IBM reported that THBP is strongly irritating to rabbit eyes and mildly irritating to rabbit skin. The company also reported that the LD50 for THBP is in excess of 5 g/kg in male rats.

Submission Evaluation

Although the submitted information indicates that THBP does possess some degree of in vitro clastogenic activity, complete copies of the final reports (including test protocols and data) from all of the studies cited in this submission should be obtained from IBM in order for EPA to evaluate more properly the reported findings.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Current Production and Use

A review of the production range (includes importation volumes) statistics for THBP (CAS No. 1143-72-2), which is listed in the initial TSCA Inventory, has shown that between 1000 and 10,000 pounds of this chemical were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed as confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information that would compromise TSCA Confidential Business Information (TSCA CBI). All of the data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

With regard to IBM's THBP production, IBM stated that THBP "is manufactured at one IBM location approximately once every three years and used in small quantities approximately twice a year with no more than 10 employees working with the material for more than two hours on each occasion for the manufacture of a photo-active substance." IBM also stated that the company "uses THBP exclusively for internal manufacturing of [the] photo-active compound." Although IBM did not report the identity of this photo-active chemical, IBM did report that THBP is reacted completely and "does not become a part of any IBM product." No information concerning any other use(s) of THBP was located by EPA in the secondary literature sources consulted.

Comments/Recommendations

In its submission, the IBM Corporation stated that the company believes that "under the actual conditions of manufacture and use, THBP represents a minimal health risk to IBM employees who handle this compound." The company also stated that employee exposure to THBP "is controlled by full protective clothing when this substance is not in a fully enclosed process."

Although a positive in vitro genotoxicity test result, when considered alone, may not be sufficient to offer reasonable support for a conclusion of substantial risk, the Agency believes that such results are of value in assessing possible risks posed by chemicals to health and/or the environment. EPA also believes that positive genotoxicity test results in combination with additional information (e.g., knowledge of potential exposure to, or high production of, the chemical substance or mixture), would suggest, in many cases, the need to conduct additional toxicity studies. The results of such studies should be considered also for possible submission to EPA pursuant to Section 8(e) of TSCA.

a) The Chemical Screening Branch (CSB/ECAD/OTS) will request the IBM Corporation to provide to EPA complete copies of the final reports (including test protocols and data) from all of the in vitro and in vivo THBP toxicity studies that were cited in IBM's submission.

In view of the Agency's general interest in corporate actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the Chemical Screening Branch will also request IBM to describe the actions IBM has taken to notify workers and others and to describe the nature of all other studies that IBM has conducted, is now conducting, or is planning to conduct to define the toxicity of and/or exposure to THBP.

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of THBP at the present time.

c) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA and ORD/EPA. A copy of this status report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0484-0511
Page 1 of 2

DATE: [redacted] 23 [redacted]

SUBJECT: Status Report* 8EHQ-0484-0511

Approved 5/23

Revision Needed ________

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The Gulf Oil Products Company provided summarized results from a battery of in vitro and in vivo genotoxicity studies of Gulf's butadiene feedstock which is reported to contain 1,3-butadiene (40-69%), 1-butene (11-19%), isobutene (5-20%), and mixed butenes and butane (7-24%). According to the submitter, the butadiene feedstock was found to be weakly positive in an in vitro primary rat hepatocyte DNA repair test, weakly positive in an in vivo mouse micronucleus test, negative in an in vitro Chinese Hamster Ovary (CHO) cell mutagenicity test, and negative in an in vitro BALB/c mouse cell transformation test.

Submission Evaluation

Although the submitted information does indicate that the tested butadiene feedstock possesses some degree of in vitro and in vivo genotoxic activity, full copies of the final reports (including protocols and data) from all of the cited studies are needed in order to evaluate the reported findings.

Current Production and Use

The Gulf Oil Products Company did not provide any information concerning the current production/importation volumes of its butadiene feedstock nor was such information located in the secondary literature sources consulted. 1,3-Butadiene is a short-chain unsaturated hydrocarbon used primarily in the manufacture of various types of synthetic rubber, plastic, and latex. According to secondary literature, the current yearly U.S. production of 1,3-butadiene is around 3 billion pounds.

Comments/Recommendations

The Gulf Oil Products Company reported that it was reviewing the "handling procedures, labeling practices and Material Safety Data Sheets to determine if any changes are needed to assure safe handling for Gulf employees, contractors, and customers."

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On January 5, 1984, EPA announced in the Federal Register (49 FR 845) that EPA had started a 180-day review of 1,3-butadiene under Section 4(f) of TSCA. This 180-day review was undertaken by EPA in order to determine "whether to initiate appropriate action to prevent or reduce risk from the chemical or to find that the risk is not unreasonable." EPA is under a statutory obligation to decide in a 180-day period whether to initiate regulatory action if EPA makes a threshold determination under Section 4(f) of TSCA that there "may be a reasonable basis to conclude that a chemical substance or mixture presents or will present a significant risk of serious or widespread harm to human beings from cancer, gene mutations, or birth defects..." On May 15, 1984, EPA published in the Federal Register (49 FR 25024) an Advanced Notice of Proposed Rulemaking (ANPR) concerning 1,3-butadiene. The following information is presented in the summary section of that ANPR:

> "This notice announces the initiation of regulatory action by EPA to determine and implement the most effective means of controlling exposures to the chemical 1,3-butadiene under the Toxic Substances Control Act (TSCA). Recent bioassays have established that 1,3-butadiene causes cancer in experimental animals. EPA, concerned about potential unreasonable risks posed mainly by occupational exposures to 1,3-butadiene, will explore regulatory options to reduce or eliminate such risks. The Occupational Safety and Health Administration (OSHA) has decided to cooperatively collect and evaluate information regarding 1,3-butadiene with EPA...."

In addition, it should be noted that the National Institute for Occupational Safety and Health (NIOSH) published (March 9, 1984) a "Current Intelligence Bulletin" in which NIOSH recommended that the current Occupational Safety and Health Administration (OSHA) workplace exposure standard of 1,000 ppm (TWA) for 1,3-butadiene be re-examined. It should also be noted that EPA's Office of Toxic Substances has received and evaluated several TSCA Section 8(e) and "For Your Information" submissions on 1,3-butadiene and has prepared a Chemical Hazard Information Profile (CHIP) on 1,3-butadiene.

a) The Chemical Screening Branch (CSB/ECAD/OTS) will request the Gulf Oil Products Company to provide to EPA complete copies of the final reports (including test protocols and data) from all of the butadiene feedstock genotoxicity studies that were cited in the company's submission.

b) The Chemical Screening Branch will provide copies of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OSWER/EPA, OW/EPA, OANR/EPA, ORD/EPA, CCD/OTS, and RMB/ECAD/OTS. A copy of this status report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: MAY 21 1984

SUBJECT: Status Report* 8EHQ-0484-0512

Approved 5/23

Revision Needed

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The Gulf Oil Products Company submitted summarized findings from a battery of genotoxicity studies of Gulfcrown Grease E.P. No. 2. According to the company, the grease was found to be positive in an *in vitro* primary rat hepatocyte DNA repair test, negative in an *in vitro* Chinese Hamster Ovary (CHO) cell mutagenicity test, negative in an *in vivo* mouse micronucleus test, and equivocal in an *in vitro* BALB/c mouse cell transformation assay.

Submission Evaluation

Although the submitted information does indicate that Gulfcrown Grease E.P. No. 2 possesses some degree of *in vitro* genotoxic activity, full copies of the final reports (including protocols and data) from all of the studies cited in the submission are needed in order to evaluate the reported findings

Current Production and Use

The Gulf Oil Products Company did not provide any information concerning the actual production or use(s) of Gulfcrown Grease E.P. No. 2 nor was such information located by the Agency in the secondary literature sources consulted.

Comments/Recommendations

In its submission, the Gulf Oil Products Company reported that it is reviewing the company's Gulfcrown Grease E.P. No. 2 "handling procedures, labeling practices and Material Safety Data Sheets to determine if any changes are needed to assure safe handling for Gulf's employees, contractors and customers."

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EPA FORM 1320-6 (REV. 3-76)

Although a positive in vitro genotoxicity test result, when considered alone, may not be sufficient to offer reasonable support for a conclusion of substantial risk, the Agency believes that such results are of value in assessing possible risks posed by chemicals to health and/or the environment. EPA also believes that positive genotoxicity test results in combination with additional information (e.g., knowledge of potential exposure to, or high production of, the chemical substance or mixture), would suggest, in many cases, the need to conduct additional toxicity studies. The results of such studies should be considered also for possible submission to EPA pursuant to Section 8(e) of TSCA.

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will request the Gulf Oil Products Company to submit complete copies of the final reports (including protocols and data) from all of the genotoxicity studies cited in the company's submission. In addition, the submitter will be requested to report the exact chemical name, CAS Registry Number (if known), and amount of each constituent in Gulfcrown Grease E.P. No. 2.

In view of the Agency's general interest in corporate actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the Gulf Oil Products Company will be requested to describe the nature of all other studies that the company has conducted, is conducting, or plans to conduct that are designed to define the toxicity of and/or exposure to Gulfcrown Grease E.P. No. 2.

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of Gulfcrown Grease E.P. No. 2 and/or its constituent(s).

c) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, CPSC, OW/EPA, OSWER/EPA, ORD/EPA, and OANR/EPA. Copies of this report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0484-0513
Page 1 of 4

DATE: MAY 29 1984

SUBJECT: Status Report* 8EHQ-0484-0513

Approved 5/30/84

Revision Needed ________

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

Mallinckrodt, Inc. submitted a complete copy of the final report of an acute rabbit dermal toxicity study of a mixture (M278) containing approximately 500 mg phenylhydroxylamine (PHA; CAS No. 100-65-2) per liter of methanol. Mallinckrodt also submitted a description of "skin effects presumed to have resulted from [worker] exposure to [a] PHA/methanol solution." In addition, the company submitted an English translation of a paper by L. Lewin entitled "The Effects of Phenylhydroxylamine. A Further Contribution to the Knowledge of Blood Poisons" (Archiv. f. Experiment. Pathol. y. Pharmakol. 35:401-414, 1895) that was cited in NIOSH's Registry of Toxic Effects of Chemical Substances (RTECS)).

The following information was contained in the Summary/Conclusion section of the submitted final report from Mallinckrodt's acute rabbit dermal toxicity study of M278 (500 mg/l PHA/methanol):

> "Undiluted M278 was applied for twenty-four hours to the intact skin of New Zealand White rabbits, weighing 2.32 to 2.98 kilograms, at dosage levels of 50, 200, 500 and 2,000 mg per kilogram of body weight (2 animals of each sex/level). Based on the limited number of animals used for the study, the acute dermal LD50 appears to be between 200 and 500 milligrams per kilogram of body weight. Complete blood counts performed on the animals at the 50 and 500 milligram per kilogram of body weight dosage levels at 1, 2, 3 and 24 hours post-application, showed at both levels, mild to moderate leukocytosis, a shift between the segmented neutrophil and lymphocyte counts and crenation and ghosting of red blood cells. Paleness and/or cyanosis of the eyes and/or mucous membranes, signs apparently related to the observed hematological abnormalities, were observed in fourteen of the sixteen animals and persisted in one survivor throughout the fourteen day observation period." (Mallinckrodt also pointed out that adverse skin, kidney, and liver effects had been observed grossly in the exposed animals).

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With regard to the adverse skin effects noted in workers exposed to a PHA/methanol solution, Mallinckrodt provided the following information:

> "During new facility start-up, Mallinckrodt workers accidently had contact with an intermediate solution containing about 500 gm/l PHA in methanol. The workers subsequently developed skin rashes/blisters/irritations of varying degrees. In some cases, the skin effects did not develop immediately but were delayed for up to 24 hours after initial contact. Healing time varied from one to several weeks."

In addition to detailing the adverse hematologic and other toxic effects observed in humans whose skin was exposed to a phenylhydroxylamine/alcohol solution, the submitted paper by Lewin contains summarized results from a number of acute toxicity studies of phenylhydroxylamine alone or mixed with alcohol administered via dermal, oral, or subcutaneous routes to rabbits, pigeons, snakes and frogs. According to Mallinckrodt, Lewin's studies showed that:

> "dermal contact of a human with PHA resulted in development of methemoglobinemia;
>
> application of PHA moistened with alcohol to the skin of a human also caused inflammation and development of nodules that finally began to subside after some 10 days;
>
> alcoholic solutions of PHA are readily absorbed;
>
> application of PHA to freshly drawn blood caused destruction of erythrocytes; and
>
> development of methemoglobinemia in experimental animals exposed to PHA was observed; subsequent reversal of the condition was attributed to decomposition of PHA following uptake of oxygen."

It should be noted that Lewin's paper also included summarized results from acute animal studies of nitrobenzene, hydroxylamine, aniline, aminophenol, p-aminophenol hydrochloride, azoxybenzene, and azobenzene.

Submission Evaluation

The submitted animal studies and human clinical case reports demonstrate that phenylhydroxylamine (PHA) in solution in alcohol penetrates the skin readily and can cause serious local and systemic toxic effects.

In addition to adverse skin effects (e.g., irritation, edema, erythema), Mallinckrodt's acute dermal toxicity study of PHA in rabbits showed that the lungs, liver, and kidneys of the exposed animals manifested systemic intoxication. The severity of the lung congestion appears to be dose-related. Methemoglobinemia and hemolysis were also observed. However, the rare cases of profound hemolysis occurred only in the low-dose group. The reported paleness and/or cyanosis of mucous membranes suggests appreciable anemia and/or interference with oxygenation of the blood. The observed cyanosis is most likely due to pulmonary congestion, rather than due to hemolysis or methemoglobinemia which did not appear to have been very severe. It should be noted that the development of methemoglobinemia will promote hemolysis by increasing erythrocyte rigidity and osmotic fragility (Lux and Glader in Beck 1977, Hematology, Page 286).

Mallinckrodt's acute rabbit dermal toxicity study of PHA appears to present the following new information with regard to toxicity: (1) a demonstration of a dose-response relationship, (b) a semi-quantitative appreciation of the extent of dermal absorption (i.e., estimated 90% absorption in 24 hours), and (c) congestion of the lungs. Lewin's paper does not mention lung congestion in animals and only implies that such an effect occurs in humans ("...rattle-like noise following respiration....") following dermal exposure to phenylhydroxylamine.

The submitted information raises a question with regard to the sensitizing potential of phenylhydroxylamine. Lewin's findings suggest that PHA is a dermal sensitizer (delayed recurring redness after recovery from PHA exposure which Lewin attributed to participation of the lymphatic system). This would tend to lower the effective dose for adverse dermal effects. There is also the possibility that PHA can cause respiratory sensitization, because PHA (like phenylethanolamine) is vasoactive. Although it has not been shown that PHA can cause constriction of bronchiolar smooth muscle, it should be noted that dyspnea (difficulty in breathing) was a common finding in the PHA-exposed animals in the Lewin and Mallinckrodt studies.

Scientifically, it would be interesting to know 1) whether PHA alone or in alcohol is a dermal sensitizer, 2) whether PHA alone or in alcohol administered by the dermal route is a respiratory sensitizer, 3) the extent of methemoglobinemia induced by PHA, and 4) the extent of PHA-induced impairment of oxygen transport in order to help sort out the relative contribution(s) of bronchiolar constriction, pulmonary congestion, hemolysis, and/or methemoglobinemia to the observed cyanosis.

Current Production and Use

A review of the production range (includes importation volumes) statistics for phenylhydroxylamine (CAS No. 100-65-2), which is listed in the initial TSCA Inventory, has shown that between 10 thousand and 101 thousand pounds of this chemical were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed as confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information that would compromise Confidential

Business Information (TSCA CBI). The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

Although Mallinckrodt did not submit any information concerning the use(s) of phenylhydroxylamine, the company did report that the chemical is a site-limited intermediate that is produced in batches via a totally enclosed process. According to secondary literature sources, phenylhydroxylamine is used to manufacture cupferron (ammonium nitroso-beta-phenylhydroxylamine), which is an analytical reagent for separating/precipitating metals such as copper and iron. Secondary literature sources also report that phenylhydroxylamine can be used in the preparation of p-aminophenol, which is a dye intermediate and a photographic developer.

Comments/Recommendations

Mallinckrodt, Inc. stated that the company has informed its workers about the toxicity of the PHA/methanol mixture and has "implemented appropriate operating procedures." In addition, Mallinckrodt reported that the "start-up conditions causing [the workers'] contact with the intermediate PHA solution have been resolved" and that "no further exposure contact is anticipated."

The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) has prepared Chemical Hazard Information Profiles (CHIPs) on nitrobenzene, aniline, p-aminophenol, p-aminophenol hydrochloride, and azobenzene. A CHIP on hydroxylamine, hydroxylamine hydrochloride, and hydroxylamine sulfate is currently in preparation. In addition, the Test Rules Development Branch (TRDB/ECAD/OTS) is evaluating toxicity and exposure information on aniline and nitrobenzene under Section 4 of TSCA as recommended by the Interagency Testing Committee (ITC).

a) In light of the the Agency's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the Chemical Screening Branch will request Mallinckrodt to describe the nature of all other studies that the company has conducted, is conducting, or plans to conduct that are designed to define the toxicity of and/or exposure to phenylhydroxylamine alone or mixed with alcohol.

b) The Chemical Screening Branch will review the reported information to determine whether further OTS assessment of phenylhydroxylamine is needed at the present time.

c) The Chemical Screening Branch will send a copy of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA, ORD/EPA, and TRDB/ECAD/OTS/OPTS. Copies of this status report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0584-0514
Page 1 of 3

DATE: JUN 8 1984

SUBJECT: Status Report* 8EHQ-0584-0514

Approved 6/14

Revision Needed

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The Celanese Corporation provided summarized results from a chronic dermal application study of n-pentanoic acid (CAS No. 109-52-4), heptanoic acid (CAS No. 111-14-8), and nonanoic acid (CAS No. 112-05-0) in C3H/HeJ mice. According to Celanese, the results indicate that there was "a significant increase in [skin] tumor incidence rate in the [n-pentanoic acid] exposed mice as compared to the control group." Celanese also reported that the results "do not show an increase in [skin] tumor incidence rate" for mice exposed dermally to heptanoic acid or nonanoic acid.

Submission Evaluation

In view of the inferences that can be drawn from knowledge about the structure-activity relationships of chemical carcinogens, the reported oncogenicity findings for n-pentanoic acid are very surprising. It should be noted that there may be at least two other plausible reasons for the observed oncogenic activity. Firstly the synthesized valeric acid used in the chronic study may have been contaminated. Although the submitted contract laboratory's protocol (standard operating procedure?) for the study indicates that the purity and stability of the test substances was to be determined by Celanese, no purity/stability information was presented in the submission. Secondly, it appears that the overall health of the mice may have been poor. The submitted information shows that the untreated C3H/HeJ mice maintained in the animal quarters had experienced a 48% mortality by the 78th week of the study. Considering that the average life-span of most mouse strains (including random-bred strains) is slightly over 2 years, the short life span of the control animals suggests that there was something toxic (oncogenic?) in the animal room environment (e.g., bedding, air, drinking-water, feed). In view of the fact that straight chain fatty acids of intermediate chain length are polar-nonpolar molecules that can act as weak promoters, it is possible that n-pentanoic acid may have acted as a promoter for some other substance to which the mice were exposed. It should also be noted that, in general, mouse skin is a very sensitive indicator of even traces of chemical substances for which this tissue is a possible target organ. Moreover, there are known initiator/promoter combinations in which the promoter, when applied to the skin, re-directs the target orientation of the initiating carcinogen to the skin (not otherwise acting on this tissue).

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Further evaluation of the reported oncogenicity findings must await EPA's receipt of a complete copy of the final report (including the actual experimental protocol, data, purity/stability information, etc.) from the chronic mouse skin application study. In addition, information about the process by which the tested n-pentanoic acid was synthesized would be of great value.

Current Production and Use

A review of the production range (includes importation volumes) statistics for n-pentanoic acid (CAS No. 109-52-4), which is listed in the initial TSCA Inventory, has shown that between 1 thousand and 11 thousand pounds of this chemical were reported as produced and/or imported in 1977. This production range information does not include any production/importation data claimed as confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information that would compromise TSCA Confidential Business Information. The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

The Celanese Corporation reported that n-pentanoic acid "is not manufactured or processed commercially by Celanese, so there is no potential for employee exposure to the material other than in occasional laboratory use." In addition, Celanese reported that it synthesized the n-pentanoic acid "on a small scale for potential end use evaulation" but did not report the nature of the end use. According to secondary literature sources, n-pentanoic acid is used as an intermediate in the manufacture of drugs, flavoring agents, perfumes, plasticizers, lubricants, and stabilizers.

Comments/Recommendations

The Celanese Corporation stated that the reported oncogenicity findings for n-pentanoic acid were being brought to the attention of the Occupational Safety and Health Administration (OSHA), the National Institute for Occupational Safety and Health (NIOSH), and the National Cancer Institute (NCI).

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will request Celanese to provide to EPA a complete copy of the final report (including the actual experimental protocol, data, purity/stability information, etc.) of the chronic mouse skin application study. The submitting company will also be requested to describe the process by which the tested n-pentanoic acid was synthesized.

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of n-pentanoic acid at the present time.

c) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, ORD/EPA, and OANR/EPA. Copies of this status report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: MAY 30 1984

SUBJECT: Status Report* 8EHQ-0584-0515 S

Approved 5/31

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section/CSB

Revision
Needed

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Note: The submitting company has claimed that its identity, the identities of the tested "epoxy finish" components, and the identity of the industrial fiber to which the finish is applied are considered to be TSCA Confidential Business Information. The Information Management Division (IMD/OTS/OPTS) has requested the submitter to substantiate all of these confidentiality claims.

Submission Description

The submitting company provided summarized results from several in vitro genotoxicity tests conducted with an epoxy finish that is described non-confidentially by the submitter as a proprietary mixture of 2 epoxy resins. According to the submitting company, "the epoxy finish gave positive results with and without activation in an Ames test, a Mouse Lymphoma test and a Sister Chromatid Exchange test."

Submission Evaluation

Although the submitted information indicates that the proprietary epoxy resin finish does possess some degree of in vitro genotoxic activity, complete copies of the final reports (including test protocols and data) are needed to evaluate the reported findings

Current Production and Use

In light of the fact that the submitting company has claimed the identities of the epoxy resin finish components to be TSCA Confidential Business Information, no production information will appear in this status report. The submitting company did report non-confidentially that the epoxy finish "is added topically to the industrial fiber at a very low concentration."

Comments/Recommendations

The submitter stated that the company is in the process of reviewing its "manufacturing process and industrial hygiene program to insure that employee protection is adequate." In addition, the submitter stated that the Occupational Safety and Health Administration (OSHA), the National Institute for Occupational Safety and Health (NIOSH), the National Cancer Institute (NCI) and the supplier of the proprietary epoxy resin mixture are being notified about the results of the genotoxicity studies. The submitter also stated that, upon receipt, the final reports of the genotoxicity studies would be transmitted to EPA.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Although a positive in vitro genotoxicity test result, when considered alone, may not be sufficient to offer reasonable support for a conclusion of substantial risk, the Agency believes that such results are of value in assessing possible risks posed by chemicals to health and/or the environment. EPA also believes that positive genotoxicity test results in combination with additional information (e.g., knowledge of potential exposure to or high production of the chemical substance or mixture), would suggest, in many cases, the need for additional toxicity studies. The results of such studies should be considered also for possible submission to EPA under Section 8(e) of TSCA.

a) The Chemical Screening Branch (CSB/ECAD/OTS) will request the submitter to ensure that EPA receives complete copies of the final reports (including protocols and data) from all genotoxicity studies cited in the submission. In addition, the submitter will be asked to report the exact chemical identity, CAS Registry Number (if known), and amount of each constituent of the tested epoxy resin finish. The submitting company will also be requested to report the exact identity of the "industrial fiber" to which the epoxy finish is applied.

   In view of EPA's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity or exposure information, the Chemical Screening Branch will request the submitting company to describe the nature of all other studies that the company has conducted, is conducting, and plans to conduct that are designed to define the toxicity of and/or the exposure to the proprietary epoxy finish or its components. In addition, the submitter will be requested to describe the actions the company has taken to notify its own workers about the reported genotoxicity findings.

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of the proprietary epoxy resin mixture and/or its components at the present time.

c) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OANR/EPA, and ORD/EPA. Copies of this status report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0584-0516 S
Page 1 of 3

DATE: JUN 8 1984

SUBJECT: Status Report* 8EHQ-0584-0516 S

Approved 6/13/84

Revision Needed ______

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Note: The submitting company has claimed its name and certain information pertaining to the intended use of the tested material as TSCA Confidential Business Information (CBI). The Information Management Division (IMD/OTS) has requested the submitting company to substantiate all of its confidentiality claims.

Submission Description

The submitting company provided a final report from an Ames test and summarized results from several other genotoxicity tests of an oxirane/methyloxirane polymer (CAS No. 9003-11-6). According to the submitter, the tested material "is the polymerization product of 26 moles oxirane and 67 moles methyloxirane" and has an average molecular weight of 5000. With regard to the results of the performed genotoxicity tests, the submitter reported that:

> "a water emulsion of the test material gave a positive response in the Ames/Salmonella Microsome Plate Test with metabolic activation. The tests were negative in the absence of the metabolic activation. In addition, preliminary reports from the same test laboratory have reported positive responses in a Mouse Lymphoma test and a Sister Chromatid Exchange test. A Cell Transformation test was negative.... A test of the article coated with the appropriate amount of the finish gave a negative response in the Ames test."

Submission Evaluation

Although the laboratory that performed the Ames/*Salmonella typhimurium* (bacteria) assay considered the oxirane/methyloxirane polymer to be mutagenic only for strain TA 98, EPA believes that a positive response was observed also with strain TA 1538. In evaluating data from Ames assays, the performing laboratory has established an arbitrary value of 3X the spontaneous reversion rate as being indicative of a positive response with strain TA 1538. Rather than rely on an arbitrary maximum response rate, it is more appropriate to look for a concentration-related response and/or a significant, reproducible response at a single concentration. In the case of the present submission, there was a reproducible, concentration-related response that in both instances reached a maximum of 2.6X the spontaneous mutation rate for strain TA 1538. This should be considered as a positive response for the tested polymer. Further, the performing laboratory conducted the Ames assay with one plate per concentration point for all strains except TA 98 which was tested with three plates per concentration point. The current Office of Toxic Substances (OTS) testing guidelines for the Ames assay recommend the use of three plates per point for all strains. The submitted final report does not offer any explanation for the unequal distribution of plates per point in this assay. In addition, the final report states that a preliminary toxicity assay showed that the polymer was toxic for the indicator organism, strain TA 100. A review of the data, however, shows that the tested polymer was virtually non-toxic at concentrations up to a maximum of 10,000 µg/plate. Overall, these particular discrepancies do not affect the Agency's evaluation and interpretation of the submitted Ames test data.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Complete copies of the final reports, including protocols and data, are needed in order to evaluate the results from the other genotoxicity assays that were cited in the submission.

Current Production and Use

A review of the production range (includes importation volumes) statistics for the oxirane/methyloxirane polymer (CAS No. 9003-11-6), which is listed in the initial TSCA Inventory, has shown that between 13.4 million and 84.3 million pounds were reported as produced and/or imported in 1977. This production range information does not include any production or importation data claimed as confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information which would compromise Confidential Business Information. The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

According to the submitting company, the oxirane/methyloxirane polymer "is being reviewed by [the submitting company in its] research and test market programs" and "is being considered for use as a finish at low levels on articles manufactured by the submitter." The submitter did not provide any information pertaining to the types of articles to which the oxirane/methyloxirane finish would be applied.

Comments/Recommendations

The submitting company stated that the manufacturer of the polymer (who was informed by the submitter about the reported genotoxicity findings) "is attempting to determine if the material itself caused the response or if the response was due to impurities, breakdown products or contaminants." In addition, the submitter stated that the reported information was sent to the Occupational Safety and Health Administration (OSHA), the National Institute for Occupational Safety and Health (NIOSH), and the National Cancer Institute (NCI). The submitter also stated that, upon receipt, copies of the final reports from the other genotoxicity assays would be transmitted to EPA and that EPA would be notified about any new significant information that the submitter receives.

Although a positive in vitro genotoxicity test result, when considered alone, may not be sufficient to offer reasonable support for a conclusion of substantial risk, the Agency believes that such results are of value in assessing possible risks posed by chemicals to health and/or the environment. EPA also believes that positive genotoxicity test results in combination with additional information (e.g., knowledge of potential exposure to or high production of the chemical substance or mixture), would suggest, in many cases, the need to conduct additional toxicologic studies. The results of such studies should be considered also for possible submission to EPA pursuant to Section 8(e) of TSCA.

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will request the submitting company to ensure that the Agency receives complete copies of the final reports (including protocols and data) from all of the genotoxicity studies cited in the submission. The submitting company will be requested also to describe the articles to which the company plans to apply the oxirane/methyloxirane finish.

In view of the Agency's general interest in corporate actions that are taken on a voluntary basis in response to chemical toxicity and/or exposure information, the submitting company will be requested to describe the nature of all other studies that it has conducted, is conducting, or plans to conduct that are designed to define the toxicity of and/or the exposure to the subject polymer. In addition, the submitting company will be asked to describe the actions it has taken to notify its workers about the reported genotoxicity information on the oxirane/methyloxirane polymer.

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of the oxirane/methyloxirane polymer.

c) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, ORD/EPA, and OAR/EPA. Copies of this status report will be sent also to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0584-0517
Page 1 of 3

DATE: [redacted] 13 [redacted]

SUBJECT: Status Report* 8EHQ-0584-0517

Approved 6/14

Revision Needed

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

Exxon Company, U.S.A. submitted summarized results from a chronic skin-painting study of a "solvent-cutback type rust-preventive" product in C3H/HeJ male mice. According to Exxon, the tested product contained Stoddard solvent (CAS No. 8052-41-3) (90.9% by volume), 2-butoxyethanol (CAS No. 111-76-2) (2.5% by volume), and a "calcium soap of oxidized wax acids blended with a minor amount of calcium petroleum sulfonate" (6.6% by volume) (the submitter stated that the supplier of these last components considers the CAS Numbers to be "trade secret"). Exxon provided the following information with regard to the results of the chronic study:

> "The lifetime mouse skin-painting study began on September 26, 1979 and ended after 864 days, which was the day of death of the last surviving animal. ["All tests were performed utilizing C3H/HeJ male mice painted with 25 microliters of material three times weekly."] At termination, 3 animals out of the original 50 (6%) had grossly diagnosed squamous cell carcinomas in or adjacent to the treatment area. During the final histopathologic examination, these tumors were confirmed by microscopic examination, and 3 additional animals were determined to have squamous cell carcinomas for a total of 6 tumor-bearing animals (12%). Also, one tumor-bearing animal had a papilloma in addition to the malignancy. Two concurrent controls, positive and negative, were also utilized in the study. The positive control, a 10% catalytic-cracked clarified oil [CAS No. 64741-62-4] in white mineral oil, U.S.P. [CAS No. 8042-47-5], elicited tumors in 48 of 50 animals (96%) by the 431st day of the test. The negative control consisted of white mineral oil, U.S.P. only, which caused no tumors during the test duration of 878 days."

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Submission Evaluation

The submitted information indicates that the tested solvent-cutback type rust-preventive product was carcinogenic to the skin of male C3H/HeJ mice. In general, it is not necessarily surprising that a product containing approximately 90% Stoddard solvent (a refined petroleum distillate with a typical boiling range of approximately 300-400°F) is carcinogenic considering the increasing body of evidence which indicates that most (if not all) petroleum derivatives may possess some degree of oncogenic or co-oncogenic potential. A complete copy of the final report, including experimental protocol and data, is needed in order to evaluate the reported oncogenicity findings properly.

Current Production and Use

Although Exxon Company, U.S.A. did not provide any information on the production volume or specific use(s) of the tested product, the company did provide the following information with regard to one component of the tested mixture:

> "As a result of Exxon's ongoing program of quality and performance evaluation of its products, one of the components [2-butoxy-ethanol] in the product tested has been eliminated from the formulation. This action was taken independently of the mouse skin painting study. Accordingly, since early in 1984, the specific product tested by skin painting is no longer being manufactured by Exxon."

Comments/Recommendations

Exxon Company, U.S.A. reported that it would "advise customers of record for this product of the results of the skin painting study and will send them a revised Material Safety Data Sheet with recommended precautions."

EPA's Office of Toxic Substances (OTS) has received and evaluated other TSCA Section 8(e) and "For Your Information" (FYI) submissions on 2-butoxyethanol, Stoddard solvent, and catalytic-cracked clarified oil. The Risk Management Branch (RMB/ECAD/OTS) has been evaluating available toxicologic and exposure information on 2-butoxyethanol and catalytic-cracked clarified oil.

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will request Exxon Company, U.S.A. to provide to the Agency a complete copy of the final report (including the experimental protocol and data) from the chronic mouse skin-painting study cited in the submission. Exxon will be asked also to provide the actual product names of the tested and new formulations.

In view of the Agency's general interest in corporate actions that are taken on a voluntary basis in response to chemical toxicity and/or exposure information, the Chemical Screening Branch will request Exxon Company, U.S.A. to describe the nature of all other studies that the company has conducted, is conducting, or plans to conduct that are designed to define the toxicity of or the exposure to the tested formulation, the new formulation (i.e., the one without 2-butoxyethanol) and/or the individual components of those products. In addition, Exxon will be asked to describe the actions it has taken to notify Exxon workers and customers of the new formulation about the reported oncogenicity findings.

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment.

c) The Chemical Screening Branch will send copies of this status report to OSHA, NIOSH, CPSC, NTP, OW/EPA, OAR/EPA, OSWER/EPA, ORD/EPA, and RMB/ECAD/OTS. Copies of this status report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: JUN 18 1984

SUBJECT: Status Report* 8EHQ-0584-0518 S

Approved 6/19/84

Revision Needed ____________

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Note: The submitting company has claimed its name and the use(s) of the tested material as TSCA Confidential Business Information. The Information Management Division (IMD/OTS/OPTS) has requested the submitting company to substantiate all of its confidentiality claims.

Submission Description

The submitting company provided summarized preliminary results from several *in vitro* genotoxicity studies of a product that is identified by the submitter as "a proprietary mixture of epoxy resins marketed under the trade name of EPON 815 (CAS No. 29407-84-9)." According to the submitter, EPON 815 produced "a positive response with and without [metabolic] activation in the Ames test, the Mouse Lymphoma test and the Sister Chromatid Exchange test." [See NOTE on Page 3 of this status report]

Submission Evaluation

Although the submitted information indicates that EPON 815 does possess some degree of *in vitro* genotoxic activity, complete copies of the final reports (including the actual experimental protocols and data) from all of the cited studies are needed in order for EPA to evaluate the reported findings.

Current Production and Use

Although the submitting company reported that its use of EPON 815 was confidential, the submission did not contain any information concerning the submitter's intended or actual use(s) of EPON 815. It should be noted that neither EPON 815 nor CAS No. 29407-84-9 were located during a review of the non-confidential portion of the TSCA Inventory. According to a publicly available on-line computerized data base (Chemical Abstacts), EPON 815 (CAS No. 29407-84-9) is a polymer comprised of bisphenol A (CAS No. 80-05-7), epichlorohydrin (CAS No. 106-89-8), and butoxymethyloxirane (CAS No. 2426-08-6). [See NOTE on Page 3 of this status report]

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Comments/Recommendations

The submitting company stated that it had notified the supplier of EPON 815, the Occupational Safety and Health Administration (OSHA), the National Institute for Occupational Safety and Health (NIOSH), and the National Cancer Institute (NCI) about the reported genotoxicity findings. The submitting company also stated that, upon receipt, copies of the final reports from the cited genotoxicity studies and "any significant new information" will be sent to EPA.

Although a positive in vitro genotoxicity test result, when considered alone, may not be sufficient to offer reasonable support for a conclusion of substantial risk, the Agency believes that such results are of value in assessing possible risks posed by chemicals to health and/or the environment. EPA also believes that positive genotoxicity test results in combination with additional information (e.g., knowledge of potential exposure to or high production of the chemical substance or mixture), would suggest, in many cases, the need to conduct additional studies. The results of such studies should be considered also for possible submission to the Agency under Section 8(e) of TSCA.

It should be noted that EPA's Office of Toxic Substances (OTS) has received and evaluated TSCA Section 8(e) and/or "For Your Information" submissions containing information on bisphenol A, epichlorohydrin, butoxymethyloxirane and other EPON resins. The Chemical Screening Branch (CSB/ECAD/OTS) has prepared a Chemical Hazard Information Profile (CHIP) on bisphenol A; the Test Rules Development Branch (TRDB/ECAD/OTS) is reviewing toxicity and exposure information on bisphenol A, epichlorohydrin, and butoxymethyloxirane; and the Risk Management Branch (RMB/ECAD/OTS) is reviewing toxicity and exposure information on epichlorohydrin and butoxymethyloxirane.

a) The Chemical Screening Branch will ask the submitter to ensure that EPA receives complete copies of the final reports (including the actual test protocols and data) from all studies cited in the submission. In addition, the submitting company will be requested to describe its actual or intended use(s) of EPON 815.

In view of the Agency's general interest in corporate actions that are taken on a voluntary basis in response to chemical toxicity and/or exposure information, the Chemical Screening Branch will request the submitting company to describe all other studies that it has conducted, is conducting, or plans to conduct that are designed to further define the toxicity of and/or the exposure to EPON 815 and any of its components. In addition, the submitting company will be requested to describe the actions that it has taken to 1) notify its workers about the genotoxic activity reported for EPON 815 and 2) reduce and/or eliminate exposure to EPON 815 or its constituents.

b) The Chemical Screening Branch will review the submitted information in order to determine the need for further OTS assessment of EPON 815.

c) The Chemical Screening Branch will send copies of this status report to OSHA, NIOSH, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OAR/EPA, ORD/EPA, IMD/OTS, TRDB/ECAD and RMB/ECAD. Copies of this status report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution.

NOTE:

In a supplemental submission (8EHQ-0684-0518 S Supplement), the Shell Oil Company provided the following information:

> "EPON Resin 815 is a mixture of about 86.5% wt. of epoxy resin (CAS No. 25068-38-6) and about 13% wt. of n-butyl glycidyl ether (n-BGE) (CAS No. 2426-08-6) [**]. Since it is a mixture, the CAS No. 29407-84-9 provided by [the submitting company] is incorrect; that CAS No. refers to a polymer of the resin and n-BGE. Shell does not manufacture, process, or sell the product corresponding to that CAS No. In EPON Resin 815, the resin and n-BGE have not reacted. EPON Resin 815 has been a commercial Shell resin for about 30 years. It is used in many applications which require a lower viscosity than that of the base epoxy resin; n-BGE is a reactive diluent used to reduce the viscosity of the base resin. EPON Resin 815 is used directly by some [Shell] customers and is formulated into proprietary products by others. In all cases, it is used in conjunction with other products such as amines, anhydrides, Lewis acids, fillers, and/or reinforcements."

In addition, the Shell Oil Company stated that in light of the known in vitro genotoxic activity of n-BGE, it is not surprising "that epoxy resins diluted with n-BGE produce an effect similar to n-BGE itself."

[**] butoxymethyloxirane

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0584-0519
Page 1 of 4

DATE: JUL 2 1984

SUBJECT: Status Report* 8EHQ-0584-0519

Approved JM 7/3/84

Revision Needed ____________

FROM: Justine Welch Schaeffer, Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The 3M Company provided summarized results from several toxicity studies conducted with a 3M research chemical and a commercial chemical that 3M processes. According to 3M, the commercial chemical, which is "purchased from American Hoechst under the trade name Pina Sensitizer KF 501 #28296", is 2,2'-[(2-carboxy-p-phenylene)bis(iminovinylene)]bis[3-ethyl]-2-thiazolium diiodide (CAS No. 20328-87-4). 3M reported that the research chemical, which is the triethylamine salt of the commercially available chemical, is the subject of a TSCA Section 5 Premanufacture Notification (PMN No. P84-688) currently under EPA review.

With regard to the toxicity of the PMN chemical, 3M provided the following information:

> "Eye Irritation Test - albino rabbits. Forty milligrams of PMN substance were applied to one eye of each of six rabbits. When the investigator returned to check the 1-hour response, all six rabbits were dead. Assuming a two to three kg body weight, the delivered dose was approximately 13-20 mg/kg. Dosing two males and two females at 5 mg/kg resulted in one male and one female death within fifteen minutes. Death was preceded by respiratory depression, prostration and mild tremors. Survivors had miosis. Dosing at 1 mg/kg did not result in death.
>
> "Acute Oral Toxicity Test - rats. Five female and five male rats were dosed with 2.5 g/kg of PMN substance. Three per sex died. Symptoms included fasiculations and tremors.
>
> "Skin Irritation Test - albino rabbits, Draize method. PMN substance was minimally irritating after placement of 0.5 g on the skin under semi-occlusion.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

"Microbial Mutagenicity Assay - Salmonella typhimurium (Ames Test). No toxicity or mutagenicity was noted with and without metabolic activation."

3M provided the following information with regard to the toxicity of Pina Sensitizer KF 501:

"Eye Irritation/Toxicity Test - albino rabbits. Three male and three female albino rabbits were dosed with 27 mg of KF 501 placed in one eye each. All three males and two females died within 15 minutes. Death was preceded by respiratory depression, prostration and mild tremors."

Submission Evaluation

It is not necessarily surprising that Pina Sensitizer KF 501 and its triethylamine salt (PMN chemical) can act qualitatively the same in terms of toxicity. The rapid lethal toxicity in albino rabbits that occurred following ocular/conjunctival administration of either chemical appears to be real, especially considering the fact that 1) the rapid lethality of the PMN chemical was found to be reproducible and dose-related and 2) the deaths of the animals exposed to either chemical were "preceded by respiratory depression, prostration, and mild tremors." It should be noted that it is unusual to see such a large disparity between the lethal dose administered by the oral (gavage) and ocular routes (the oral LD50 for the PMN chemical appears to be approximately 2 g/kg; in the eye the LD50 for the PMN chemical is about 5 mg/kg). The LD100 via the ocular route is estimated to be 13-20 mg/kg for the PMN chemical and approximately 27 mg/kg for the commercial chemical.

While the negative irritancy and mutagenicity findings reported for the PMN chemical are of interest in their own right, they shed little light on the lethality observed in rabbits. The lack of difference in the Ames test with and without activation does not rule out the possibility of a first-pass detoxification by the liver in rats following oral administration.

The possibility exists that absorption could occur also via the oral or nasal mucous membranes. In addition, it is possible that enhanced dermal absorption could occur through the action of solvents or other agents that may damage skin.

Current Production and Use

The commercial chemical substance (Pina Sensitizer KF 501) was not located during a review of the non-confidential portion of the TSCA Inventory. In its submission, 3M stated that 3M uses Pina Sensitizer KF 501 "in very small quantities as a dye component for a specialized graphic arts film." In addition, 3M provided the following worker exposure information:

> "At present no more than 15 3M workers are involved in processing the subject chemical in both powder and solution form and handling dried coated film. To date less than 1.0 kg of [KF 501] has been handled in the plant. Hygienic handling procedures and precautions have been reviewed and augmented as follows:
>
> a. In addition to disposable impervious gloves and coveralls, powdered form handlers who make up the solution for coating will wear air-line continous flow helmet respirators rather than half-mask dust respirators, safety goggles rather than safety glasses and will continue to use filtered local exhaust ventilation.
>
> b. Solution handlers, who handle the 0.33% dye solution in methanol, will wear safety goggles instead of safety glasses, and continue to wear gloves (to be disposed immediately after use) and use filtered local exhaust.
>
> c. Coater operators who may come into contact with the coating solution which contains 0.18 mg/g of emulsion will wear safety glasses and gloves.
>
> "[3M does] not believe persons handling [the] dry coated film product are at risk. The coating on the film is composed of only 0.01% of the substance which is equivalent to a coating weight of 8.0 mg/m^2. The dye is not expected to leach during normal contact. [3M] has done extraction tests to verify this. When extracted in 0.9% saline buffered at pH 7.3, no dye was detected at a delection limit of 1.0 µg/ml. The amount which could have been extracted was 13 µg/ml."

Although the 3M Company's Section 8(e) submission did not contain any information concerning 3M's planned production volumes or use of the PMN chemical, PMN No. P84-688 stated that the PMN chemical would be produced in quantities of 4-8 kg per year and used "as a sensitizing dye in lithographic plates."

Comments/Recommendations

In addition to the previously mentioned safe handling changes, 3M reported that the company plans to conduct additional toxicologic studies on the commercial and PMN chemicals. Specifically, 3M stated that the planned studies would involve 1) "lower dosing in the acute oral toxicity test depending on the availability of the test [PMN] compound", 2) "acute dermal toxicity evaluation of the 0.33% dye solution in methanol with both the [PMN compound and KF 501]", and 3) "ocular toxicity of film developer containing dye." In addition, 3M stated that the toxicity findings for the PMN compound were reported previously to EPA's Chemical Control Division (CCD/OTS/OPTS). 3M also stated that American Hoechst was notified about the toxicity of Pina Sensitizer KF 501 and would communicate further the need for safe handling.

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will request the 3M Company to provide complete copies of the final reports (including the experimental protocols and data) from all of the performed and planned studies on Pina Sensitizer KF 501 that were cited in the company's Section 8(e) submission. (The Chemical Control Division will be requesting the 3M Company to provide additional information concerning the PMN substance).

In light of EPA's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity and/or exposure information, the Chemical Screening Branch will ask American Hoechst to describe the actions that it has taken to 1) warn workers and others, and 2) reduce and/or eliminate exposure to Pina Sensitizer KF 501. American Hoechst will also be asked to describe the nature of all other studies that it has conducted, is conducting, or plans to conduct that are designed to define the toxicity of and/or the exposure to Pina Sensitizer KF 501.

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of Pina Sensitizer KF 501.

c) The Chemical Screening Branch will send copies of this status report to OSHA, NIOSH, CPSC, NTP, FDA, OSWER/EPA, OW/EPA, OAR/EPA, ORD/EPA, CCD/OTS and IMD/EPA. Copies of this report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0684-0520
Page 1 of 3

DATE: JUL 11 1984

SUBJECT: Status Report* 8EHQ-0684-0520

Approved 7/12

Revision
Needed

FROM: James F. Darr, Acting Section Head JFD
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The CIBA-GEIGY Corporation provided a copy of the final report from a 28-day rat oral toxicity study of 2-methyl-1-[(4-methylthio)phenyl]-2-(4-morpholinyl)-1-propanone (Irgacure® 907; CAS No. 71868-10-5). CIBA-GEIGY presented the following information with regard to the results of the performed study:

> "The test material, Irgacure® 907, was administered daily by gavage [to groups of 5 male/5 female rats] at dose levels of 0, 30, 100, and 300 mg/kg of body-weight for 28 days. The observations of greatest concern toxicologically were seen at the high dose level only (300 mg/kg/day) and consisted of pale/opaque eyes (6 of 10 animals) and lameness of hind legs (8 to 10 animals). As clarified in oral dicussions with the investigators, the notation of "opaque eyes" indicates likely corneal opacity and "lameness of hind legs" is indicative of transient paralysis of the hind legs. As noted above, these effects were observed only at the highest dose (a level that caused the death of 3 of 10 rats) when administered by a route which has little relevance to the human experience."

Submission Evaluation

Although the reported "hind limb lameness" suggests a neurotoxic action, the final report does not note the intensity, time of onset, or duration (other than the use of the term "transient") of the observed paralysis. It is apparent that the study did not include any histopathologic examination of the nervous system. Although the lack of such an examination is quite common in classical sub-acute toxicity studies, a thorough examination of the nervous system in the case of the 28-day study of Irgacure® 907 could have yielded information important for understanding the apparent neurotoxic activity of the chemical.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Although it is known that certain chemicals when administered via non-ocular routes can produce corneal opacities and/or other deleterious effects in the eyes, such findings are not common.

In addition to the transient hind limb paralysis in 8/10 rats, corneal opacity in 6/10 rats, and death of 3/10 rats, the animals in the 300 mg/kg group exhibited salivation, diarrhea, ruffled fur, hair loss, and emaciation; these signs were not observed in the animals in the lower dose groups. In addition, there was a significant and dose-dependent mean body weight loss in both male and female rats in the 100 and 300 mg/kg dose groups, and a dose-dependent decrease in mean food consumption for males in the 100 and 300 mg/kg dose groups and for females in the 30, 100, and 300 mg/kg dose groups. Metabolic and hematologic disturbances were also observed in males and females in the 300 mg/kg dose group.

With regard to the submitter's statement that the oral route of exposure used in the 28-day study of Irgacure® 907 "has little relevance to the human experience," it should be noted that the normal body clearance mechanisms for inhaled materials such as dusts or mists can and in many cases do involve swallowing.

Current Production and Use

The CIBA-GEIGY Corporation reported that Irgacure® 907 "was the subject of a [TSCA Section 5] Premanufacture Notification, PMN No. 84-35, for which a Notice of Commencement (of importation) was submitted to EPA on February 22, 1984." CIBA-GEIGY also reported that Irgacure® 907 "is in a very early stage of commercialization" and "only limited quantities have thus far been distributed." With regard to the uses of and potential exposure to Irgacure® 907, CIBA-GEIGY presented the following information:

> "Irgacure® 907 is used as a high extinction photoinitiator in UV curable inks and coatings. It is added to pigment concentrates or to monomer/oligomers in such quantitites that the use level is between 0.5 to 5.0% based on finished ink or coating. In view of the nature of some of the other coating ingredients, workers are likely to be wearing gloves and respirators or dust masks, limiting actual exposure. Once incorporated into the cured ink or coating, exposure to Irgacure® 907 is essentially precluded."

Comments/Recommendations

CIBA-GEIGY reported that in response to the observed toxicity it had 1) revised the Irgacure® 907 label and Material Safety Data Sheet (MSDS) and 2) notified workers and customers. (Copies of the customer notification letters and revised Irgacure® 907 MSDS and product label were provided in the submission.)

a) In view of EPA's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity or exposure information, the Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will request the CIBA-GEIGY Corporation to describe the nature of all other studies that the company is conducting or plans to conduct that are designed to define the toxicity of and/or exposure to Irgacure® 907.

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of Irgacure® 907.

c) The Chemical Screening Branch will send copies of this status report to OSHA, NIOSH, FDA, CPSC, NTP, OSWER/EPA, OW/EPA, OAR/EPA, ORD/EPA, CCD/OTS and IMD/OTS. Copies of the report will also be provided to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: SEP 5 1984

SUBJECT: Status Report* 8EHQ-0884-0524

Approved 9/5/84

FROM: James F. Darr, Acting Section Head James F. Darr
Chemical Risk Identification Section/CSB

Revision Needed ______

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The Union Carbide Corporation provided summarized results from a sub-chronic rat inhalation study of gamma-methacryloxypropyltrimethoxysilane (Silane A-174; CAS No. 2530-85-0). According to Union Carbide, "the results of this study in rats indicate that repeated exposure to moderately high concentrations of a respirable aerosol of hydrolysis and condensation products derived from an aqueous solution of Silane A-174 caused a chronic inflammatory reaction which was localized to the larynx...." In addition, Union Carbide provided the following information with regard to the performed study:

> "Fischer 344 rats were used in groups containing 18 males and 18 females. Groups were exposed to the aerosol for 6 hours a day, 5 days a week, for 14 weeks. The mean concentrations of aerosol solids to which three groups were exposed were 244, 100 and 50 mg/m^3. The aerosol was generated from a 15% aqueous solution of hydrolysis and condensation products of Silane A-174, and the average mass median aerodynamic diameter was 1.6 microns and therefore the droplets were respirable. A control group of animals, for comparative purposes, was exposed to chamber air alone. Shortly after the final exposure period, 10 male and 10 female rats from all aerosol-exposed groups and the control group were sacrificed. The remaining animals were kept for a 14-week post-exposure observation period. Animals were observed daily for signs of toxicity, and weighed weekly during the exposure period. During the post-exposure period, the rats were weighed weekly for the first four weeks, and thereafter on alternate weeks. Additionally, food and water consumption were measured, analyses performed, and various clinical chemistry and hematological analyses performed. Immediately following sacrifice at the ends of both the exposure periods and the post-exposure periods, animals were subjected to autopsy and a large variety of tissues removed for examination by light microscopy."

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: AUG 27 [illegible]

8EHQ-0784-0521 S
Page 1 of 6

SUBJECT: Status Report* 8EHQ-0784-0521 S

Approved 8/20/84

FROM: James F. Darr, Acting Section Head James F Darr
Chemical Risk Identification Section/CSB

Revision Needed ____ ______

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

On behalf of the Mallory Capacitor Company Division of Emhart Industries, Inc., the Emhart Corporation provided the following information concerning the detection of polychlorinated biphenyls (PCBs) at concentrations that were in many cases in excess of 50 parts per million (ppm):

> "The Mallory [Capacitor Company] Division operates a facility for the production of electronic components, including capacitors, at Belew Circle, Waynesboro, Tennessee 38485. The building was acquired by the former owner, P. R. Mallory & Co., Inc., in 1968, and the business of manufacturing capacitors has been carried on at that location up to the present time. Polychlorinated biphenyls (PCBs) were used in the manufacture of capacitors at this facility until 1978. When the use of PCBs was discontinued at the plant, the then owner of the facility, P. R. Mallory & Co. Inc., conducted a clean-up of equipment at the facility to remove PCBs. [The] Emhart Corporation purchased certain assets of P. R. Mallory & Co., Inc., in 1979, including the Waynesboro, Tennessee facility, and a second clean-up of PCBs at the facility was conducted at that time. The facility currently holds an NPDES [i.e., National Pollutant Discharge Elimination System] permit for discharge of stormwater run-off containing PCBs...." [A copy of the NPDES permit was contained in the Emhart Corporation's submission.]
>
> "In testing wastes generated at the facility prior to submitting them for recycling, it was recently discovered that certain of the wastes contained PCBs. Further testing of those wastes and associated process equipment indicated that there might be PCBs present in the Waynesboro facility. Accordingly, a program of testing was undertaken to determine the source and extent of any PCBs at the Waynesboro facility. The results of this testing program showed that PCBs are present at the facility in various locations and concentrations."

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> "...PCBs have been found to be present in the pump oil used at the facility and in trichloroethylene solvent still bottoms generated by the facility's solvent distillation unit. In investigating this situation, the company has discovered that waste pump oil has been sold to oil companies and others for recycling or burning as fuel, and that the solvent still bottoms have been shipped to Chemical Waste Management in Emelle, Alabama for land disposal. In addition, the pumps at the facility are vented to the atmosphere, and preliminary test results have shown PCBs to be present in the exhaust. Preliminary results have also indicated that PCBs are present on the roof and in soil outside the facility."

According to the submitted information, PCBs were also detected in a number of drums located in Hebron, Ohio.

Production and Use of PCBs

Polychlorinated biphenyls (PCBs; CAS No. 1336-36-3) are members of a broad family of organic chemicals known as chlorinated hydrocarbons. PCBs have heavy oil-like consistencies and weigh approximately 10-12 pounds per gallon. PCBs are characterized by a high degree of chemical stability, low solubility in water, high solubility in fat, low flammability, low electrical conductivity, and high boiling points. These physical/chemical properties have made PCBs commercially attractive.

Although PCBs can be produced naturally in the environment, almost all PCBs in existence today have been manufactured synthetically. The primary uses of PCBs were, and continue to be, electical transformer cooling liquids and capacitor dielectric fluids. Most of the PCBs marketed in the U.S. are still in service in these applications. However, PCBs have also been used in a variety of other applications such as heat transfer systems and hydraulic fluids; dye carriers in carbonless copy paper; plastizers in paints, adhesives, and caulking compounds; fillers in investment casting wax; and as dust control agents, sealants, and coatings on roads.

Submission Evaluation

The very characteristics of PCBs that make them commercially attractive also make their environmental and health effects of significant concern. Once released into the environment, the more highly chlorinated PCBs decompose very slowly over a period of several decades. Due to this chemical stability, PCBs remain in the environment and can be taken up by organisms and accumulated in fatty tissues. In man, PCBs can enter the body via the lungs, gastrointestinal tract and skin; circulate throughout the body; and be stored in adipose tissue.

PCBs can be hazardous to health at extremely low levels; animal studies have shown that PCBs can cause toxic effects in many species at doses in the low parts per million (ppm) range. In well documented tests with laboratory animals, PCBs have been shown to cause reproductive failures, gastric disorders, skin lesions, tumors, and developmental toxicity. The limited epidemiological data which are available indicate that the animal studies are predictive of potential adverse effects of PCBs on human health.

Legislative and Regulatory Actions on PCBs

A report by the President's Council on Environmental Quality (CEQ) in May of 1972 recommended that Congress enact the Toxic Substances Control Act (TSCA) to provide the regulatory authority required to deal with PCBs and other chemicals. Before the passage of TSCA, EPA could only regulate facilities that discharged PCBs into navigable waterways. On February 2, 1977, the Agency promulgated a final rule (42 FR 6532) under Section 307(a) of the Federal Water Pollution Control Act (FWPCA) banning the discharge of PCBs into waterways by electrical transformer and capacitor manufacturers.

When the Toxic Substances Control Act was passed in 1976, there was widespread concern about the potential adverse effects of PCBs on the environment and human health. Congress responded to this problem by designating PCBs for regulation in Section 6(e) of TSCA. Specifically, the provisions of Section 6(e):

- prohibit the use of PCBs after January 1, 1978;
- prohibit the manufacture of PCBs after January 1, 1979;
- prohibit PCB processing and commercial distribution after July 1, 1979;
- create two exceptions under which EPA may, by rule, allow the use of PCBs to continue by finding that:
  1) the use of PCBs is in a "totally enclosed" manner, and
  2) the activity "will not result in an unreasonble risk of injury to health or the environment" (for uses of PCBs in other than a "totally enclosed" manner); and
- provide for the adequate marking and disposal of PCBs still in use.

TSCA Section 6(e)(3)(B) provides further that the Administrator may, by rule, grant an exemption from the general ban on the manufacture, processing and distribution in commerce of PCBs upon finding that an unreasonable risk of exposure is not present and that good faith efforts have been made to develop substitutes for the PCBs.

Since the passage of TSCA, EPA has implemented the Section 6(e) provisions by phased rulemaking:

On February 17, 1978, EPA promulgated the PCB Marking and Disposal Rule (43 FR 7150) that established specific requirements for the marking and disposal of PCBs according to the nature and concentration of the PCBs in question.

On May 31, 1979, the Agency promulgated the PCBs Manufacturing, Processing, Distribution in Commerce, and Use Prohibitions (PCB Ban Rule; 44 FR 31514). In addition to implementing the major provisions of Section 6(e) of TSCA, this rule:

° established a regulatory cutoff of 50 ppm for PCBs;

° authorized the use of PCB-containing electrical equipment by finding such uses to be "totally enclosed;"

° authorized eleven other miscellaneous uses which EPA found would not present an unreasonable risk of injury to health or the environment; and

° amended the PCB Marking and Disposal Rule.

In 1980, the Environmental Defense Fund, Inc. (EDF) sucessfully challenged EPA's 50 ppm regulatory cutoff and the finding that the use of PCBs in electrical equipment was "totally enclosed." Since then, EPA has promulgated court ordered rulemaking in order to adress the aspects of the PCB Ban Rule overturned in EDF vs. EPA.

On August 25, 1982, EPA promulgated the final PCB Electrical Use Rule (47 FR 37342) amending the portions of the original PCB Ban Rule dealing with electrical equipment. This rule authorized the use of PCBs in eight categories of electrical equipment in accordance with use and servicing restrictions specified for each category. The use authority for the eight categories is not based upon a finding that the activities are "totally enclosed." Rather, EPA found that these uses would not present an unreasonable risk. The PCB Electrical Use Rule did stipulate that electrical equipment containing PCBs which may pose an unreasonable risk of exposure to food or animal feed are not allowed after 1988.

The EDF vs. EPA court decision invalidated the 50 ppm cutoff for regulation of PCBs. Therefore, EPA promulgated two rules to deal with PCBs at concentrations of less than 50 ppm (primarily PCBs that are produced as undesired byproducts of other chemical processes).

On October 21, 1982, EPA promulgated the Closed and Controlled Waste Manufacturing Rule (47 FR 46980). Under this rule, a manufacturing process may be excluded from regulation under Section 6(e) of TSCA if the process meets the criteria for:

- "closed manufacturing processes" (i.e., those processes that produce PCBs in concentrations below limits of quantitation (LOQ) for specified media, such as waste streams, ambient air, effluent water and products); or
- "controlled waste manufacturing processes" (i.e., those that produce PCBs in the waste stream above the LOQ but concentrations below the LOQ in all other media).

On July 10, 1984, EPA promulgated the Uncontrolled PCBs Rule (49 FR 28173) which excluded from the general ban those manufacturing processes that inadvertantly produce PCBs below an annual average of 25 ppm, not exceeding a maximum of 50 ppm at any time. These manufacturing processes are subject to other criteria and disposal requirements specified in the rule.

On July 10, 1984, EPA also issued a Final Exemptions Rule (49 FR 28154) acting on 109 petitions for exemption from the prohibition against the manufacture, processing and distribution in commerce of PCBs. EPA granted 58 of these petitions and granted one other petition in part after making the determination that the proposed activities do not pose an unreasonable risk of injury to health or the environment and that good faith efforts were made by the petitioners to develop a PCB substitute. Of the 109 petitions, 49 were denied and one was dismissed. Action on an additional 49 petitions was deferred pending further EPA evaluation based on the Uncontrolled PCBs Rule.

The July 10, 1984 rulemakings (49 FR 28183-28202) also authorized the use of PCBs:

- in small quantities for research and development (R&D) (small quantities for R&D is defined as PCBs that are 1) originally packaged in hermetically sealed containers of a volume of no more than 5 milliliters, and 2) used only for purposes of experimentation on or analysis of PCBs but not for research or analysis for the purpose of developing a PCB product);
- in hydraulic and heat transfer fluids at concentrations below 50 ppm;
- in compressors and condensates of natural gas pipelines at concentrations below 50 ppm;
- as a mounting medium;
- as a low fluorescence immersion oil; and
- as an optical fluid.

The use authorizations listed above are based upon the Agency's determination that such uses do not pose unreasonable risks to human health or the environment.

Comments/Recommendations

In its Section 8(e) notice, the Emhart Corporation stated that "further investigations are being conducted to determine the amount of wastes sent off site and their disposition so that appropriate action can be taken to assure proper handling of these wastes." The Emhart Corporation also reported that the company "has contracted with outside environmental consultants and assigned its environmental personnel to deal in a proper manner with this situation."

The Office of Toxic Substances has received a number of TSCA Section 8(e) and "For Your Information" (FYI) submissions that have contained information on PCBs (8EHQ-0778-0209, 8EHQ-1079-0319, 8EHQ-0180-0330, 8EHQ-0780-0352, 8EHQ-0981-0413, 8EHQ-0982-0457, FYI-AX-0878-0006 and FYI-OTS-1081-0140).

a) Immediately upon receipt of Emhart Corporation's Section 8(e) notice, the Chemical Screening Branch (CSB/ECAD/OTS) sent copies of the 8(e) notice to EPA Region IV and V, the Chemical Regulation Branch (CRB/EED/OTS/OPTS), the Office of Water (OW/EPA) and to the Compliance Monitoring Staff (CMS/OPTS) for appropriate followup action. The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, OW/EPA, OSWER/EPA, ORD/EPA, OAR/EPA, Region IV and V, CRB/EED/OTS/OPTS, and CMS/OPTS. Copies of this status report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0784-0522
Page 1 of 3

DATE: AUG 27 1984

SUBJECT: Status Report* 8EHQ-0784-0522

Approved Jh 8/22/84

FROM: James F. Darr, Acting Section Head James F. Darr
Chemical Risk Identification Section/CSB

Revision Needed ______

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The Witco Chemical Corporation provided the final reports from a battery of in vitro genotoxicity studies that had been conducted with a mixture of the following two chemical substances:

7-Oxabicyclo[4.1.0.]heptane-3-carboxylic acid
7-oxabicyclo[4.1.0.]hept-3-ylmethyl ester
(CAS No. 2386-87-0); and

Phosphorous acid, isodecyl diphenyl ester
(CAS No. 26544-23-0).

According to the submitter, the tested mixture exhibited in vitro genotoxic activity in the Ames Salmonella typhimurium (bacteria) Assay, the Mouse Lymphoma Cell Forward Mutation Assay, and the Chinese Hamster Ovary (CHO) Cell Sister Chromatid Exchange (SCE) Assay.

Submission Evaluation

Although the submitted final reports did not include the actual experimental protocols for the performed studies, it does appear that the tested mixture induced an increased revertant frequency in Salmonella typhimurium strain TA 1535 in the presence of exogenous metabolic activation, induced an increased mutation frequency in cultured mouse lymphoma cells both with and without activation, and induced an increased number of Sister Chromatid Exchanges (SCEs) in cultured CHO cells both with and without activation.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Current Production and Use

A review of the production range (includes importation volumes) statistics for CAS No. 2386-87-0, which is listed in the initial TSCA Inventory, has shown that no 1977 production/importation was reported or that all of the production range data reported were claimed as TSCA Confidential Business Information (TSCA CBI) by the manufacturer(s) and/or importer(s) and cannot be disclosed (Section 14(a) of TSCA, U.S.C. 2613(a)). The data submitted for the TSCA Inventory, including the production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

A review of the production range (includes importation volumes) statistics for CAS No. 26544-23-0, which is also listed in the initial TSCA Inventory, has shown that between 1.2 and 12 million pounds were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed as TSCA CBI by the person(s) reporting for the initial TSCA Inventory nor does it include any information that would compromise TSCA CBI. All of the data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

According to the submitter, the mixture is a "non-volatile, non-distillable liquid" which is used at a concentration of "0.1 to 0.15% in polycarbonates as a color stabilizer." With regard to possible exposure to the mixture, the submitter stated that:

> "The only situation where exposure to the undiluted mixture may occur is through accidental skin contact during manufacture or during handling while being incorporated into polycarbonate resin. [The company believes] that any potential health hazards would be well protected against by observing commonly used industrial hygiene practices. This includes wearing protective clothing, safety goggles and impervious gloves. Any potential exposure to the general public from the tested mixture is likely to be extremely small [because the mixture] is used at low levels and is bound up in a non-volatile, insoluble polycarbonate resin."

No further information concerning the use(s) of the individual chemicals or the mixture itself was located by the Agency in any of the secondary literature sources consulted.

Comments/Recommendations

In its submission, the Witco Chemical Corporation stated that it was notifying its employees and customers about the reported *in vitro* genotoxicity findings.

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will request the Witco Chemical Corporation to provide a complete copy of the actual experimental protocol used for each in vitro genotoxicity study that was cited in the company's submission. In addition, Witco will be asked to report the exact amount of each of the chemicals in the tested mixture.

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of the subject mixture or its components.

c) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, FDA, CPSC, NTP, OW/EPA, OSWER/EPA, ORD/EPA and OAR/EPA. Copies of this status report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: AUG 27 1984

SUBJECT: Status Report* 8EHQ-0884-0523 and
8EHQ-0884-0523 Supplement

Approved 8/28/84

Revision Needed ____

FROM: James F. Darr, Acting Section Head James F. Darr
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The Velsicol Chemical Corporation provided complete copies of a preliminary draft report (8EHQ-0884-0523) and final report (8EHQ-0884-0523 Supplement) of a cohort mortality study of workers employed at Velsicol's Chattanooga, Tennessee facility between 1943 and 1982. The "Summary" section of the final report presented the following information concerning the results of the study:

> "The cohort of this historical prospective mortality study consisted of 697 male employees at Velsicol Chemical Corporation's chlorination plant in Chattanooga. A majority of the cohort was potentially exposed to benzotrichloride [CAS No. 98-07-7], benzyl chloride [CAS No. 100-44-7], benzoyl chloride [CAS No. 98-88-4], and other related chemicals. The mortality experience of the cohort was observed from 1943 through 1982. Vital status follow-up showed that 622 (89.24%) were alive, 47 (6.74%) were deceased, and 28 (4.02%) were of unknown status as of 31 December 1982. Among those identified as deceased, death certificates were obtained for 44 (93.62%). Underlying causes of death were coded according to the International Classification of Diseases. Cause-specific mortality analyses were based on the U.S. male population as comparison.
>
> "For the cohort as a whole, no statistically significant mortality excess was detected. The overall Standardized Mortality Ratio (SMR) was 100.3 and the SMR for all cancers combined was 121.6; neither was significantly different from the expected value of 100, based on the U.S. male mortality experience. Contrary to the finding reported by Sorahan et al (1983), no death from cancer of the digestive system occurred among the cohort. The respiratory cancer SMR for the Chattanooga cohort as a whole was 246.3 (7 observed vs. 2.84 expected). The excess was of borderline statistical significance, the lower 95% confidence limit being 98.9. Analysis by race showed that all 7 respiratory cancer deaths came from the white male employees, with an SMR of 264.5, statistically signficant at the 0.05 level. The respiratory cancer mortality excess was higher among

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

employees in maintenance (SMR = 228.7) than among those in operations or production (SMR = 178.2). The lung cancer mortality excess among the laboratory employees was statistically significant (SMR = 1292.5). However, this observation should be viewed with caution, since it was based on only two deaths. Further analysis indicated that the respiratory cancer mortality excess was limited to white male employees with 15 or more years of employment (SMR = 388.8, statistically significant). Analysis by major chemical exposure showed that employees potentially exposed to benzotrichloride, benzyl chloride and/or benzoyl chloride experienced significantly increased risk of respiratory cancer. However, it should be pointed out that the majority of cohort was potentially exposed to all these three, as well as to other chemicals present at the plant. The finding on respiratory cancer was consistent with those reported by Sakaba et al (1976), Sakaba and Fukuda (1977), Sorahan et al (1983), and Rockette and Arena (1983). For other causes of death, the study did not suggest an increased risk for the Chattanooga cohort.

"Major limitations of the study included the small study size and the lack of smoking history, as well as other occupational and environmental exposure information. Without smoking history information for the entire cohort, the contribution of cigarette smoking to the observed respiratory cancer excess could not be quantitatively evaluated. However, based on animal data as well as other epidemiological studies, together with the internal consistency of analysis by length of employment, the data suggested an association between the chlorination process of toluene at the Chattanooga plant and an increased risk of respiratory cancer...."

The following references were cited in the above summary:

Rockette and Arena (1983), Mortality Patterns of Workers in the Niagra Plant. Report Submitted to Hooker Chemical Company

Sakabe et al (1976), Cancer Among Benzoyl Chloride Workers. Ann NY Acad Sci 271, 67-70.

Sakabe and Fukuda (1977), An Updating Report on Cancer Among Benzoyl Chloride Manufacturing Workers (letter). Ind. Health 15, 173-174

Sorahan et al (1983), A Mortality Study of Workers in a Factory Manufacturing Chlorinated Toluenes. Ann Occup Hyg 27, 173-182

Submission Evaluation

The preliminary draft report and the final report of the cohort mortality study have been transmitted to the Risk Management Branch (RMB/ECAD/OTS) for inclusion into its ongoing review of available toxicity/exposure data on chlorinated toluenes.

Production and Use

A review of the production range (includes importation volumes) statistics for the subject substances, which are listed in the TSCA Inventory, has shown that the following amounts were reported as produced/imported in 1977:

Chemical Name	CAS Number	Approximate Prod./Import. Range
Benzoyl Chloride	98-88-4	10 million to 52 million pounds
Benzyl Chloride	100-44-7	52 million to 110 million pounds
Benzotrichloride	98-07-7	10 million to 50 million pounds

The above ranges do not include any production/importation data claimed as confidential by the person(s) reporting for the TSCA Inventory, nor do they include any information which would compromise TSCA Confidential Business Information (TSCA CBI). The data submitted for the TSCA Inventory, including the production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 FR 710).

Benzoyl chloride is used as a chemical intermediate in the acylation of alcohols, phenols and amines, and in the manufacture of benzoyl peroxide and certain dye intermediates. Benzyl chloride is used as a chemical intermediate in the manufacture of benzyl compounds, perfumes, pharmaceuticals, dyes, synthetic tannins and artificial resins. Benzotrichloride is used mainly in the manufacture of synthetic dyes and other organic chemicals, including some types of pesticides.

According to Velsicol, "the subject chemicals are produced and, where used by Velsicol, used in a completely closed system except during sampling, loading and unloading." In addition, Velsicol reported that the results of an industrial hygiene survey had shown that "during routine operations the levels of worker exposure were below 1 ppm." Velsicol also reported, however, that "in one case where a worker was repairing a leak in the benzoyl chloride process, exposures reached 1 ppm."

Comments/Recommendations

Velsicol reported that the company has notified its own workers and the National Institute for Occupational Safety and Health (NIOSH) about the findings of the submitted cohort mortality study. In addition, Velsicol reported that the company had "recommended that [the subject] chemicals "be handled as suspect carcinogens and recommended the use of protective clothing and respirators." Velsicol also reported that "in order to remove a major source of potential exposure," the company had "renovated the Quality Control Laboratory at the Chattanooga Plant" and that the "renovation included upgrading of the air handling system, ventilation and laboratory hoods." Finally, Velsicol reported that the company plans to notify its customers about the submitted findings and plans to conduct further investigations in order to obtain "a more definitive answer to the specific question of whether long term exposure to the subject chemicals did result in an increase of lung cancer."

The Office of Toxic Substances (OTS/OPTS/EPA) has received and evaluated several TSCA Section 8(e) and "For Your Information" (FYI) submissions that have presented toxicity/exposure data on benzoyl chloride, benzyl chloride, and benzotrichloride, as well as other chlorinated toluenes. In addition, Chemical Screening Branch (CSB/ECAD/OTS) has prepared Chemical Hazard Information Profiles (CHIPs) on benzoyl chloride, benzyl chloride, and benzotrichloride.

a) The Chemical Screening Branch will request the Velsicol Chemical Corporation to keep EPA abreast of the results of Velsicol's further investigations into the possible relationship between long term human exposure to the subject chemicals and lung cancer.

b) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OSWER/EPA, OW/EPA, OAR/EPA, ORD/EPA, OPP/OPTS, and RMB/ECAD/OTS. Copies of this status report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution.

> "No deaths occurred during the study and, apart from a decrease in the rate of gain in body weight during exposure of the male rats exposed to 250 mg/m^3, there were no signs of toxicity. No significant differences between controls and aerosol-exposed animals were seen with respect to urinalysis, hematology and clinical chemistry. The only histopathological findings were treatment-related upper respiratory tract lesions in all three exposure groups. There was hyalinization of the epithelial cells of the olfactory mucosa and, of most biological significance, the presence of a granulomatous reaction in the larynx. The granulomatous reaction was focal, often associated with formation of polyps projecting into the lumen of the larynx, and was present with a similar incidence and severity at all three exposure concentrations. Also, the chronic inflammatory lesion was still present following a 14-week post-exposure recovery period."

Union Carbide reported that "the scientists responsible for the conduct of the study and for the interpretation of the test results believe that the production of the granulomatous reaction was positively related to exposure to a respirable aerosol derived from Silane A-174." In addition, Union Carbide stated that "although certain aspects of the conduct of the study do not reflect in-use practices with Silane A-174, for example the use of a more concentrated aqueous solution favoring polymerization and therefore a foreign body reaction," Union Carbide considered it appropriate to report the findings under Section 8(e) of TSCA "because of the chronic inflammatory nature of the lesion and its anatomical localization."

With regard to the interpretation of the practical significance of the submitted findings, Union Carbide reported that "it is relevant to note that there was an indication of a laryngeal granulomatous reaction in a pilot study involving a 9-day exposure to the aerosol, but no such laryngeal pathology was apparent following a 9-day exposure to the vapor from Silane A-174." Union Carbide also stated that the findings from the pilot study suggest that the hazard indicated by exposure to Silane A-174 "is specific to a respirable aerosol and not a factor in vapor exposure."

Finally, Union Carbide stated that the company "has no evidence or knowledge of any untoward health effects associated with over 20 years of manufacture and marketing of Silane A-174, either of a kind implied by the testing results or of any other kind."

Submission Evaluation

Although it is not necessarily suprising that Silane A-174 and its hydrolysis products would be highly irritating to respiratory tract tissue, it is important to note that 1) the granulomatous lesions of the larynx, which were found in many cases to be associated with polyps, were observed in the animals exposed to all Silane A-174 concentrations tested, and 2) the granulomatous lesions were still present at the end of a 14-week post-exposure observation period. It should also be noted that granulomatous lesions of the larynx have been observed in humans as the result of trauma associated with intratracheal intubation.

Further evaluation of the sub-chronic inhalation study findings should be possible upon EPA's receipt of a complete copy of the final report which should include a full copy of the experimental protocols and data. In addition, the submitter should be asked to provide a complete copy of the final report, including test protocols and data, from the 9-day pilot inhalation study that was cited in the submission. It would also be of interest to know the pH of the test samples.

Current Production and Use

A review of the production range (includes importation volumes) statistics for CAS No. 2530-85-0, which is listed in the initial TSCA Inventory, has shown that between 0 and 1000 pounds were reported as produced/imported in 1977. This 1977 production range information does not include any production/importation data that was claimed as TSCA Confidential Business Information (TSCA CBI) by the person(s) reporting for the TSCA Inventory, nor does it include any information that would compromise TSCA CBI. All of the data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

Although Union Carbide did not provide any information concerning its current production of Silane A-174, the company did provide the following information with regard to the use of and potential exposure to the chemical:

> "Silane A-174 is used in industrial applications as a coupling agent, principally in the manufacture of coated glass fiber materials and objects, in which use the chemical loses its identity and is converted into a matrix material. In a pilot industrial hygiene study at an actual use location, concentrations up to 0.68 mg/m^3 of total material (only part of which was derived from Silane A-174) were found, which are seen to be an order of magnitude lower than the lowest level used in the animal studies."

No further information concerning the production or use of the subject chemical was located in the secondary literature sources consulted by EPA.

Comments/Recommendations

In the cover letter to its submission, Union Carbide stated that the company "intends to undertake further studies to define the conditions necessary for development of the granulomatous lesion, and, if necessary, to develop measures to protect employees from potential respiratory tract injury resulting from exposure to respirable aerosols derived from Silane A-174." In addition, Union Carbide stated that the company is "advising its employees who are involved in the manufacture and handling of Silane A-174, its customers, and other producers" of the chemical about the reported findings. Union Carbide also stated that upon completion of the final report from the sub-chronic inhalation study, a copy of that report will be sent to the Agency.

a) The Chemical Screening Branch (CSB/ECAD/OTS) will request the Union Carbide Corporation to ensure that EPA receives a complete copy of the final report (including the actual experimental protocol(s) and data) from the sub-chronic Silane A-174 inhalation study that was cited in the submission. In addition, Union Carbide will be requested to submit a complete copy of the final report (including the actual experimental protcol(s) and data) from the 9-day inhalation study with Silane A-174 that was cited in the initial submission.

b) The Chemical Screening Branch will review the reported information to determine the need for further OTS assessment of the subject chemical substance.

c) The Chemical Screening Branch will transmit copies of this status report to NIOSH, OSHA, CPSC, NTP, OW/EPA, OAR/EPA, OSWER/EPA, and ORD/EPA. Copies of this report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0884-0525
Page 1 of 2

DATE: SEP 5 1984

SUBJECT: Status Report* 8EHQ-0884-0525

Approved 9/6/84

FROM: James F. Darr, Acting Section Head James F. Darr
Chemical Risk Identification Section/CSB

Revision
Needed ______

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

On behalf of the U.S. producers of methylene chloride (CAS No. 75-09-2), the Halogenated Solvents Industry Alliance (HSIA) submitted summarized "preliminary, and as yet unverified" results from a National Toxicology Program (NTP) bioassay of methylene chloride which was administered via inhalation to male and female F344 rats at doses of 0, 1000, 2000, or 4000 ppm and to male and female B6C3F1 mice at doses of 0, 2000, or 4000 ppm. According to the submitted information, the preliminary results of the bioassay (which is currently in the histopathology phase) "indicate that methylene chloride induces a very high incidence of lung and liver tumors in both sexes of mice."

Submission Evaluation

The submitted information has been transmitted to the Test Rules Development Branch (TRDB/ECAD/OTS) and the Risk Management Branch (RMB/ECAD/OTS) for inclusion in their ongoing review of available toxicologic and exposure data on methylene chloride.

Current Production and Use

A review of the production range (includes importation volumes) statistics for methylene chloride (CAS No. 75-09-2), which is listed in the initial TSCA Inventory, has shown that between 350 million and 1.4 billion pounds were reported as produced/imported in 1977. This production range information does not include any information claimed by the manufacturer(s) and/or importer(s) as TSCA Confidential Business Information (TSCA CBI) nor does it include any information that would compromise TSCA CBI. All data submitted for the TSCA Inventory, including the production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

According to secondary literature sources, the U.S. production of methylene chloride was approximately 530 million pounds in 1983.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information

EPA FORM 1320-6 (REV. 3-76)

Methylene chloride has uses in paint removers; propellants for aerosol sprays; blowing agents in foam; plastics processing; and solvent degreasing and extraction procedures.

Comments/Recommendations

The Office of Toxic Substances (OTS) has received and evaluated other TSCA Section 8(e) and "For Your Information" submissions that have contained toxicologic and/or exposure information on methylene chloride.

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will receive (directly from NTP) a complete copy of the draft technical report from the methylene chloride inhalation study as soon as the report is formally released by NTP for peer review by the Technical Report Peer Review Subcommittee of NTP's Board of Scientific Counselors. According to NTP staff, the draft technical report will be available in the spring of 1985.

b) The Chemical Screening Branch will transmit a copy of this status report to NIOSH, OSHA, CPSC, FDA, OW/EPA, OSWER/EPA, OAR/EPA, ORD/EPA, TRDB/ECAD and RMB/ECAD. A copy of this status report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS/EPA) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0384-0526
Page 1 of 3

DATE: SEP 10 [illegible]

SUBJECT: Status Report* 8EHQ-0884-0526

Approved FDK 9/10/84

Revision Needed ____________

FROM: James F. Darr, Acting Section Head James F. Darr
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The Union Carbide Corporation provided summarized results from a chronic mouse skin application study of a mixture of unsaturated aliphatic oils (C16-32). According to the submitter, there were "a small number of [late developing] neoplasms at the site of [recurrent] application of the test material...." Union Carbide presented the following details concerning the performed study:

> "Three groups, each containing 50 mice of the C3H/HeJ strain were used. One group of mice had a 50% (v/v) solution of Aliphatic Oils in acetone applied to the skin, the second received acetone alone (negative control), and the third received 0.1% methylcholanthrene in acetone (positive control). Each mouse received 25 µl of solution on each treatment day. Applications were made to the hair-clipped dorsal skin, three times a week until death. Necropsy was performed on all animals dying and on sacrificed moribund survivors. All animals have now died, and histological confirmation of tumor types has been undertaken."
>
> "In the group of 50 animals receiving Aliphatic Oils, three animals each developed a squamous cell carcinoma at the site of application of the test material. One of these animals also had systemic lymphosarcoma. Additionally, a fourth animal with lymphosarcoma had a metastatic deposit at the site of application of the test material. The relationship of the latter effect to treatment is uncertain. The first squamous cell carcinoma was diagnosed at 526 days (i.e., 75 weeks) from the first application of Aliphatic Oils. With the acetone control group, one mouse developed a subcutaneous fibrosarcoma in the area of acetone application. A high incidence of squamous cell carcinomas developed early in the group of mice treated with methylcholanthrene."

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

EPA FORM 1320-6 (REV. 3-76)

"The incidence of malignant neoplasms was low, and their latency to detection long, following recurrent application of Aliphatic Oils to mouse skin.... Comparison of the incidence and latency of these neoplasms with those developing in the methylcholanthrene-treated animals would suggest that Aliphatic Oils are of low potency with respect to dermal carcinogenic potential."

Submission Evaluation

The submitted information does indicate that the tested material displays a weak carcinogenic activity toward the skin of C3H/HeJ mice. The provided spectral analysis information shows that 3 types of double bonds are present in the mixture (i.e., pendant methylene, terminal vinyl, and internal trans-vinylidene). It should be noted that double bonds may react with certain functional groups in key cellular macromolecules by Michael addition and/or can undergo epoxidation through metabolism. Therefore, the reported findings are consistent with the concept that double bonds are "soft" electrophiles that can confer oncogenic activity on an otherwise non-oncogenic molecule.

Current Production and Use

The Union Carbide Corporation provided the following information concerning the use of and the potential for exposure to the test material:

> "The test substance is an oil that is intermediate in the process of polymerizing ethylene by the low-pressure process. Except for interrupting the continuous process by which polyethylene is manufactured, the intermediates are not isolated and hence did not qualify for reporting to the TSCA Inventory. The stimulus for testing the material was from a concern to understand any potential biological properties in the event [the material was] to be isolated or released by either deliberately or inadvertently interrupting the process. Spectral data indicate [that the aliphatic oils] are aliphatic hydrocarbons, unsaturated with pendant methylene groups, terminal vinyl groups, and (principally) internal trans-vinylidene unsaturation - spectra consistent with being telomers of ethylene. They are predominantly in the C16-C32 range. The chemicals are neither isolated or used for any particular purpose. ...Union Carbide licenses the process for manufacturing polyethylene...."

Comments/Recommendations

In its submission, Union Carbide reported that its licensees are being notified about the submitted findings. In addition, Union Carbide reported that "full details of the study will be made available upon completion of the report and conclusion of the Quality Assurance process." It was also reported that "no further toxicological studies are anticipated with this material."

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will ask the Union Carbide Corporation to ensure that EPA receives, immediately upon completion, a full copy of the final report (including the actual experimental protocol(s) and data) from the company's chronic mouse skin application study of unsaturated aliphatic oil (C16-C32).

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of C16-C32 unsaturated aliphatic oil.

c) The Chemical Screening Branch will transmit copies of this status report to NIOSH, OSHA, NTP, OW/EPA, OSWER, OAR/EPA, and ORD/EPA. Copies of this status report will also be provided to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0884-0527
Page 1 of 2

DATE: SEP 7 1984

SUBJECT: Status Report* 8EHQ-0884-0527

Approved 9/10/84

FROM: James F. Darr, Acting Section Head James F. Darr
Chemical Risk Identification Section/CSB

Revision Needed ____________

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

On behalf of its American members, the International Chlorinated Paraffin Producers Testing Consortium submitted summarized preliminary findings from a study of "C-14/17, 52% chlorinated, chlorinated paraffin (CAS No. 63449-39-8)" administered in the feed to pregnant rats "prior to and during gestation and during lactation." According to the submitter, at the highest dose tested (6250 ppm), "there was subcutaneous bleeding and death in rat pups, but the dams apparently were not affected."

The submitter reported that "exposure to humans under similar circumstances is not foreseeable, and based on use and handling experience, similar human health hazards are highly unlikely." The submitter also stated that "chlorinated paraffins have been produced commercially for several decades" during which time "there has never been an indication of any adverse health effects

Submission Evaluation

The submitted information has been transmitted to the Test Rules Development Branch (TRDB/ECAD/OTS) and the Risk Management Branch (RMB/ECAD/OTS) for inclusion in their ongoing review of available toxicologic and exposure information on chlorinated paraffins.

Current Production and Use

A review of the production range (includes importation volumes) statistics for CAS No. 63449-39-8, which is listed in the initial TSCA Inventory, has shown that between 27 million and 170 million pounds were produced/imported in 1977. This production range information does not include any data claimed as TSCA Confidential Business Information (CBI) by the person(s) reporting for the Inventory, nor does it include any data that would compromise TSCA CBI. The data submitted for the TSCA Inventory, including the production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

The chlorinated paraffins are a family of chlorinated compounds that are derived from primarily saturated, straight-chain hydrocarbons. The maximum amount of chlorination that is achievable is 70% by weight. In general, the chloroparaffins are viscous liquids with the viscosity increasing as the percent chlorine increases. These compounds are considered to be soluble in oils and oil solvents, insoluble in water, readily emulsifiable and nonflammable. Chlorinated paraffins are used as fire retardants, as plasticizers and as additives in extreme pressure lubricants. It should be noted that chlorinated paraffins are used in some applications as substitutes for polychlorinated biphenyls (PCBs), a class of compounds that are strictly regulated by EPA.

Comments/Recommendations

The submitter stated that the final report from the ongoing rat study will be forwarded to EPA upon completion of the statistical analysis and data audit. In addition, the submitter stated that other studies will be conducted in accordance with a Negotiated Testing Agreement under Section 4 of TSCA.

EPA has received and evaluated several TSCA Section 8(e) notices that have contained toxicity and/or exposure information on the chlorinated paraffins.

a) The Chemical Screening Branch will request the submitter to ensure that EPA receives, immediately upon completion, a full copy of the final report including the actual test protocol, statistical analyses, and data from the feeding study that was cited in the submission.

b) The Chemical Screening Branch will transmit a copy of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OSWER/EPA, OW/EPA, OAR/EPA, ORD/EPA, TRDB/ECAD/OTS and RMB/ECAD/OTS. A copy of this status report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0884-0528
Page 1 of 3

DATE: SEP 11 1984

SUBJECT: Status Report* 8EHQ-0884-0528

Approved 9/11/84

FROM: James F. Darr, Acting Section Head James F. Darr
Chemical Risk Identification Section/CSB

Revision Needed ______

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The Dow Chemical Company submitted summary results from a number of toxicologic studies of 2-phenoxyethanol (CAS No. 122-99-6) in rabbits. The submitter provided the following information with regard to the results of the performed tests:

> "A dermal probe teratology study in pregnant New Zealand white rabbits was conducted at [2-phenoxyethanol] dose levels of 0, 300, 600 and 1000 mg/kg/day with 10 rabbits per group. The animals were treated on days 6 through 19 of gestation. Necropsy was conducted on day 19 of gestation. No unexpected results were observed."
>
> "In the full dermal teratology study using the same test species [New Zealand white rabbits] and dose levels, but with 20 rabbits per group, a total of 9 high dose (1000 mg/kg/day) and 4 middle dose (600 mg/kg/day) rabbits died or were killed in moribund condition following 5 to 13 applications of 2-phenoxyethanol. Many of these rabbits died showing signs of hematologic changes indicative of the breakdown of red blood cells characterized by hemoglobinuria, pale livers, dark red-black kidneys and dark red-black urine in the bladder. As a result of this excessive mortality, the 1000 mg/kg dosing was discontinued and all remaining high dose animals were sacrificed. The remaining animals in the 300 mg/kg and 600 mg/kg groups continued treatment and will be examined for teratologic effects. Hematologic parameters were monitored in these animals on day 19 of gestation (the day after dosing was completed). The survivors did not exhibit any hematologic changes, and no deaths or signs of toxicity were observed in the low dose (300 mg/kg/day) animals. Teratologic data have not been tabulated or evaluated to date."
>
> "To confirm the hematologic effects observed in the maternal animals in the teratology study, a seperate 2-week toxicity study was initiated wherein 10 female (non-pregnant) rabbits were given 2-phenoxyethanol via the dermal route at a dose

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

level of 1000 mg/kg/day for a planned 14 days. Concurrently, five control rabbits received distilled water daily via the dermal route. In this study, 7 of the 2-phenoxyethanol treated rabbits either died or were killed in moribund condition between 5 - 8 days of treatment, indicating that non-pregnant animals are also sensitive to the hemolytic effects of 2-phenoxyethanol. Each of these rabbits exhibited signs which were similar to those of the affected animals in the teratology study, the prominent sign being hematologic changes indicative of red blood cell breakdown. The three surviving rabbits treated with 2-phenoxyethanol did not exhibit hematologic changes."

Submission Evaluation

The submitted information has been transmitted to the Test Rules Development Branch (TRDB/ECAD/OTS/OPTS) for inclusion in their ongoing evaluation of toxicologic and exposure information on 2-phenoxyethanol, a chemical recommended by the Interagency Testing Committee (ITC) for testing consideration by EPA under Section 4 of TSCA.

Current Production and Use

A review of the production range (includes importation volumes) statistics for 2-phenoxyethanol (CAS No. 122-99-6), which is listed in the initial TSCA Inventory, has shown that between 1 million and 10 million pounds of this chemical were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed to be TSCA Confidential Business Information (TSCA CBI), nor does it include any information that would compromise TSCA CBI. All of the data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

In its submission, Dow stated that "the major use of 2-phenoxyethanol is as a paint coalescing agent in latex paints." Dow also stated that the minor applications of 2-phenoxyethanol include "cleaners, polishes, photographic developers, and cosmetics."

Comments/Recommendations

Dow reported in its submission that its employees, customers, and the co-sponsors of the teratology study were being notified about the submitted toxicologic findings. In addition, Dow stated that although its "current work practices are not expected to result in exposures at the levels where toxicity was first noted in these studies," the company plans to review its work practices to ensure that workers exposed occupationally to 2-phenoxyethanol are taking appropriate precautions with regard to skin contact.

EPA's Office of Toxic Substances (OTS) has received and evaluated several TSCA Section 8(e) and/or "For Your Information" (FYI) submissions containing toxicologic and/or exposure information on a number of glycol ethers, including 2-ethoxyethanol (and its acetate), 2-methoxyethanol (and its acetate), and 2-butoxyethanol (and its acetate). The Chemical Screening Branch (CSB/ECAD/OTS) has prepared Chemical Hazard Information Profiles (CHIPs) on 2-methoxyethanol and its acetate, and 2-ethoxyethanol and its acetate. The Risk Management Branch (RMB/ECAD/OTS) is currently evaluating the available toxicologic and exposure data on a number of glycol ethers.

a) The Chemical Screening Branch (CSB/ECAD/OTS) will request the Dow Chemical Company to provide a complete copy of the final report, including the actual experimental protocol and data, from each toxicity study that was cited in the submission.

b) The Chemical Screening Branch will transmit a copy of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OSWER/EPA, OW/EPA, OAR/EPA, ORD/EPA, TRDB/ECAD/OTS, and RMB/ECAD/OTS. Copies of the status report will also be sent to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0984-0529
Page 1 of 5

DATE: SEP 27 1984

SUBJECT: Status Report* 8EHQ-0984-0529

Approved 9/28

FROM: James F. Darr, Acting Section Head James F. Darr
Chemical Risk Identification Section/CSB

Revision Needed

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The Eastman Kodak Company submitted summarized results from a subchronic feeding study of 1-phenyl-3-pyrazolidinone (phenidone; CAS No. 92-43-3) in rats. The company provided the following information with regard to the performed study:

> "Male and female rats were exposed to phenidone in the diet for either 42 (hereafter referred to as the interim group) or 90 days. The interim groups consisted of 10 rats of each sex while those fed for 90 days contained 20 rats of each sex. Target doses were 0.02, 0.08, and 0.32 percent in the diet. Estimated doses for the interim group males were 12, 59, and 244 mg/kg/day; for the females estimated doses were 13, 61, and 270 mg/kg/day. Estimated doses for males in the 90-day study were 9, 46, and 214 mg/kg/day; for females, estimated doses were 10, 51, and 239 mg/kg/day."
>
> "Males and females in the 0.08% and 0.32% groups showed retarded weight gains and lower final body weights; 0.02% in the diet had no effect on weight gains or final body weights. Feed consumption was reduced in both males and females at 0.08% and 0.32% although not for every time period; changes in feed consumption were minor and transient at 0.02%."
>
> "Hematologic effects were observed in males and females from both the interim and 90 day groups in a dose-related manner. Two types of effects were observed: 1) a mild anemia with Heinz bodies, macrocytosis and increased hemoglobin in red cells, and 2) an increase in platelet counts and white cells. Animals ingesting the diet with 0.02% phenidone showed very slight hematologic effects. Serum clinical chemistries were variable; the changes were of no toxicological significance."

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

"Changes in organ weights were observed, but were mainly attributed to decreased body weights. Target organ effects based on organ weight changes were enlargement of spleens at 0.08% and 0.32% (both interim and 90 day groups) in males and females and testicular atrophy in males at 0.32% (both interim and 90 day groups). No toxicologically significant effects on organ weights were observed at 0.02%."

"Gross and/or histopathological changes were observed in a dose-related manner in the spleen, liver, kidneys, testes, and epididymides, as follows:

Liver	0.32%	Kupffer cell hemosiderosis; extramedullary hematopoiesis (except interim males).
	0.08%	Kupffer cell hemosiderosis (except interim males); extramedullary hematopoiesis (90 day females only).
	0.02%	No effects.
Kidneys	0.32%	Proximal tubule cell pigmentation; tubular casts (interim females only); increased severity of hyalin droplet degeneration (interim males only).
	0.08%	Proximal tubule cell pigmentation (interim female and 90 day male only).
	0.02%	No effects.
Spleen	0.32%	Increased congestion, hemosiderosis, extramedullary hematopoiesis, and red pulp atrophy.
	0.08%	Increased congestion, hemosiderosis, extramedullary hematopoiesis, and red pulp atrophy only in female interim and 90 day groups.
	0.02%	Increased congestion and hemosiderosis (equivocal in all groups except interim males where there was no hemosiderosis).
Testes	0.32%	Atrophy and degeneration of seminiferous tubules.
	0.08%	Atrophy of seminiferous tubules (only in 1 of 10 males of the interim group).
	0.02%	No effects.
Epididymides	0.32%	Contains degenerating spermatozoa and decreased or absence of mature spermatozoa.
	0.08%	No effects.
	0.02%	No effects."

Eastman Kodak also stated that "with the exception of dermatitis, [the company is] "not aware of any advserse health problems associated with the use of [phenidone] or solutions containing this chemical."

Submission Evaluation

The reported adverse effects are most probably real (treatment-related) in that they were dose-related. Although the lower food consumption observed in the two highest dosage groups (0.08% and 0.32%) may mean that the chemically treated food was less palatable, these groups apparently did receive higher doses judging from the more severe effects that were found. The observed hemosiderosis (i.e., the excess storage of iron/hemosiderin) in the spleen and in the Kupffer cells (macrophages) of the liver and the observed but unspecified pigmentation of the proximal convoluted tubules of the kidney suggests the development of a hemolytic disorder. This is supported by the finding of mild anemia and macrocytosis. Although an increase in white blood cells and platelets was also reported, it is not clear that this increase was absolute or due to a decrease in circulating blood volume. It would be of interest to know the results of a differential white-cell count as well as the specific gravity of the urine. The finding of Heinz bodies in the red cells suggests that some of the hemoglobin was changed to methemoglobin. It is not clear whether the observed atrophy of the red splenic pulp was a direct toxic effect or was secondary to an attempted compensation for the loss of oxygen-carrying capacity caused by hemolysis which resulted in exhaustion of the red pulp of the spleen.

Dose-related degenerative changes were noted in the seminiferous tubules of the testes, as well as in the spermatozoa in the epididymides. It is not clear that these changes were direct toxic effects or resulted from impaired nutrition (either general malnutrition from decreased food consumption or local impairment of nutrition of stored spermatozoa as the result of damage to the epididymides). Although it is possible that phenidone produces its diverse toxic effects via several different mechanisms, it could be speculated that there may be a common factor involved between the observed hemolytic effects and the observed testicular atrophy. In addition, it should be noted that phenidone can inhibit the metabolism of arachidonic acid to prostaglandins, and hydroperoxy fatty acids (Fischer et al, Carcinogenesis, 1982, 3:1243-1245). It is not clear whether or how the inhibition of arachidonic acid metabolism plays a role in toxic action(s) of phenidone.

It should be noted that the submitting company's statement with regard to dermatitis differs from the information contained in the Merck Index (9th Edition, 1976, page 951) which indicates that dermatitis has not been experienced following exposure to phenidone. One might infer from this disparity that if phenidone is irritating to the skin, it may be only weakly irritating.

Further evaluation of the reported toxicologic findings for phenidone should be possible upon the Agency's receipt of a complete copy of the final report (including the experimental protocol and data).

Current Production and Use

A review of the production range (includes importation volumes) statistics for phenidone (CAS No. 92-43-3), which is listed in the initial TSCA Inventory, has shown that between 131 thousand and 1.31 million pounds were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed as TSCA Confidential Business Information (TSCA CBI) by the person(s) reporting for the TSCA Inventory, nor does it include any information that would compromise TSCA CBI. All data reported for the TSCA Inventory, including production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

In its submission, the Eastman Kodak Company reported that it does not manufacture phenidone. The company stated that "the major use of the purchased material is as a minor component in the formulation of x-ray developer solutions." In addition, the company stated that small amounts of phenidone "are also used as minor components in the formulation of a few commercial photographic developer products." According to secondary literature sources, phenidone is used also as a laboratory reagent.

Comments/Recommendations

Eastman Kodak stated that its supplier has been informed about the reported toxicologic findings on phenidone. In addition, Eastman Kodak stated that, upon completion, EPA will receive a copy of the final report from the company's subchronic phenidone study.

a) The Chemical Screening Branch (CSB/ECAD/OTS) will request the Eastman Kodak Company to ensure that, upon completion, EPA receives a full copy of the final report (including the actual experimental protocol and data) from the subchronic phenidone feeding study that was cited in the submission.

Considering the Agency's general interest in corporate actions that are taken on a voluntary basis in response to chemical toxicity/exposure data, the Chemical Screening Branch will ask Eastman Kodak to describe the actions the company has taken to reduce and/or eliminate exposure to phenidone. In addition, the Eastman Kodak Company will be asked to describe the nature of all other studies that the company has conducted, is conducting, or plans to conduct that are designed to determine the toxicity of and/or the exposure to phenidone.

b) The Chemical Screening Branch will review the submitted information in order to determine the need for further OTS assessment of phenidone.

c) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OSWER/EPA, OW/EPA, OAR/EPA, and ORD/EPA. In addition, copies of the status report will be sent to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-0984-0530
Page 1 of 3

DATE: SEP 17 1984

SUBJECT: Status Report* 8EHQ-0984-0530

Approved [illegible]

Revision Needed ______

FROM: James F. Darr, Acting Section Head James F. Darr
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

E. I. Du Pont de Nemours & Company, Inc. submitted summarized preliminary results from a 2-year inhalation study of titanium tetrachloride (CAS No. 7550-45-0) in rats. The submitter provided the following information with regard to the study:

> "Under the conditions of the test, 100 male and 100 female Charles River-CD rats were exposed to titanium tetrachloride ($TiCl_4$) vapors at exposure levels of 0, 0.1, 1 or 10 mg/m^3, for 6 hours a day, 5 days a week. Exposure atmospheres were generated by passing a stream of nitrogen through liquid titanium tetrachloride at ambient temperature. This saturated vapor was diluted with humidified air and fed into the exposure chamber. Since titanium chloride reacts with the moisture in the air, this generation procedure resulted in an atmosphere containing primarily particulate and gaseous titanium tetrachloride hydrolysis products. These particulates were 100% respirable with a mass median diameter of approximately 0.4 microns."
>
> "A total of 20 rats per group were sacrificed at 3, 6, and 12 months to evaluate chronic toxicity. No unusual effects were observed in these rats. The surviving rats were sacrificed at the end of the 104 week exposure period. All major tissues and organs were evaluated and, except for the respiratory tract, were normal. In the lungs, histopathological examination revealed tumors at the 10 mg/m^3 exposure level. These tumors were keratinized, cystic squamous cell carcinoma (one male and one female) and squamous cell carcinoma, differentiated (one male and two female). No compound-related tumors were seen at lower exposure levels. In addition, inflammation typical of nuisance dust exposure, predominantly at the higher exposure levels, was observed." [The submitter provided draft tables of the reported respiratory tract findings.]

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

In its submission, Du Pont stated that titanium tetrachloride, which is a liquid at room temperature, is known to be highly irritating to skin and eyes. In addition, Du Pont stated that the chemical is highly toxic via inhalation (4-HR LC50 of 460 mg/m^3 in rats). Du Pont also stated that titanium tetrachloride was non-mutagenic in a Chinese Hamster Ovary (CHO) cell/HGPRT assay and in a *Bacillus subtillis* rec-assay.

Finally, Du Pont stated that "...preliminary indications from a brief review of medical records indicate that the employees in [Du Pont's] manufacturing operations in which titanium tetrachloride is made, experienced no statistically significant increase in incidence of mortality from lung cancer."

Submission Evaluation

The submitted information suggests that titanium tetrachloride, at the highest tested dose only, displays marginal oncogenic activity toward the lung tissue of Charles River-CD rats. Further evaluation of the findings should be possible upon the Agency's receipt of a full copy of the final report which should include the actual experimental protocol and data.

Current Production and Use

A review of the production range (includes importation volumes) statistics for titanium tetrachloride (CAS No. 7550-45-0), which is listed in the initial TSCA Inventory, has shown that between 250 million and 1.1 billion pounds of this chemical were reported as produced/imported in 1977. This production range information does not include any production/importation data that was claimed as TSCA Confidential Business Information (TSCA CBI) by the person(s) reporting for the TSCA Inventory, nor does it include any information that would compromise TSCA CBI. The data submitted for the TSCA Inventory, including production range data, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

According to secondary literature sources, titanium tetrachloride is used as a mordant, as a catalyst in polymerization reactions, and as a raw material for titanium metal. In addition, titanium tetrachloride is used in the manufacture of iridescent glass, artificial pearls, and titanium pigments.

Comments/Recommendations

In its submission, Du Pont stated that in light of the reported findings the company has 1) "established a workplace exposure level of 0.5 mg/m^3 (8- and 12-hour Time Weighted Average)," and 2) "communicated the test results and [Du Pont's] assessment of their meaning to [Du Pont] employees and to other agencies (OSHA, NIOSH)." In addition, Du Pont stated that the company plans to notify Du Pont's customers and competitors about the reported bioassay results and Du Pont's assessment of the meaning of the findings. Du Pont also stated that the company plans "to determine the feasibility of conducting an epidemiology study of those employees in [Du Pont's] manufacturing plants who have the potential for exposure to titanium tetrachloride during their normal plant duties...." Finally, Du Pont stated that copies of the final report of the 2-year titanium tetrachloride rat inhalation bioassay would be provided to EPA and other government agencies.

a) The Chemical Screening Branch (CSB/ECAD/OTS) will request Du Pont to ensure that EPA receives, immediately upon completion, a full copy of the final report (including the actual experimental protocol and data) from Du Pont's 2-year inhalation study of titanium tetrachloride. Du Pont will also be requested to provide a complete copy of the final report (including the actual experimental protocol and data) from each in vitro mutagenicity assay that was cited in the submission.

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of titanium tetrachloride.

c) The Chemical Screening Branch will transmit copies of this status report to NIOSH, OSHA, CPSC, NTP, OW/EPA, OAR/EPA, OSWER/EPA, and ORD/EPA. Copies of this status report will be sent also to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: OCT 2 1984

SUBJECT: Status Report* 8EHQ-0984-0531 S

Approved 10/2/84

Revision Needed ______

FROM: James F. Darr, Acting Section Head James F. Darr
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

NOTE: The submitting company has claimed its name and the exact identity of the subject chemical to be TSCA Confidential Business Information (TSCA CBI). The submitter reported non-confidentially that the subject chemical is a fatty acid imidazoline listed in the TSCA Inventory under the following CAS No.: 68442-97-7. According to Volume I of the TSCA Inventory, CAS No. 68442-97-7 pertains to 2-nor-tall-oil alkyl derivatives of 4,5-dihydro-1H-imidazole-1-ethanamine. Staff of the Information Management Division (IMD/OTS/OPTS/EPA) will request the submitting company to substantiate all of its claims of confidentiality.

Submission Description

The submitting company provided summarized results from several acute *in vivo* toxicity studies of the fatty acid imidazoline. According to the submitter, the chemical was found to be severely irritating to skin (species not specified) and corrosive (site and species not specified), and to have an oral LD50 of approximately 5 g/kg in rats (6 of 10 rats died during days 2 through 6 following oral administration).

Submission Evaluation

On the basis of the reported LD50 of approximately 5 g/kg, the tested chemical would be classified as being only slightly to moderately toxic via the oral route of administration. The pH of the subject chemical (which is expected to be high (i.e., basic)) may be responsible for the observed irritation/corrosion. The submitter should be asked to report the pH (if known) for the tested chemical substance. In addition, a complete copy of the final report (including experimental protocol and data) from each acute toxicity study that was cited in the submission should be requested.

NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Current Production and Use

A review of the production range (includes importation volumes) statistics for CAS No. 68442-97-7, which is listed in the initial TSCA Inventory, has shown that no 1977 production/importation was reported or that all of the production range data reported were claimed as TSCA Confidential Business Information (TSCA CBI) by the manufacturer(s) and/or importer(s) and cannot be disclosed (Section 14(a) of TSCA; U.S.C. 2613(a)). The data submitted for the TSCA Inventory, including the production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

In its submission, the company reported that the "fatty acid imidazoline is being developed as a competitive product for use as a corrosion inhibitor in the petroleum industry" and "exposures to the substance are minimal as use is in closed systems." The submitter also stated that "similar products with similar ingredients have been in commercial use for approximately 25 years without reports, known to [the submitting company], of adverse effects."

Comments/Recommendations

It should be noted that it has been EPA's longstanding position that certain types of acute animal toxicity information may not warrant submission to EPA under Section 8(e), the "substantial risk" information reporting provision of the Toxic Substances Control Act (TSCA). The basis for EPA's position is as follows:

> The preface to Part V of the Agency's March 16, 1978, TSCA Section 8(e) policy statement ("Statement of Interpretation and Enforcement Policy; Notification of Substantial Risk" 43 FR 11110) states that "a substantial risk of injury to health or the environment is a risk of considerable concern because of (a) the seriousness of the [adverse] effect...and (b) the fact or probability of its occurrence." With regard to the seriousness of the effect, Part V explains that the Agency considers the health effects for which substantial risk information must be reported to include "any pattern of effects or evidence which reasonably supports the conclusion that the chemical substance or mixture can produce cancer, mutation, birth defects, or toxic effects resulting in death, or serious or prolonged incapacitation." Information with respect to these effects can be obtained directly or inferred from designed studies (i.e., in vivo experiments as described in Part VI of the Section 8(e) policy statement). With regard to the criterion concerning the "fact or probability" of the occurrence of such effects, Part V of the Section 8(e) policy statement explains that certain types of health effects are so serious that relatively little weight should be given to the chemical's exposure in determining whether a risk is substantial.

EPA's response to Comment 14 in Appendix B of the Section 8(e) policy statement provides guidance concerning the 8(e)-applicability of results obtained from routine acute in vivo range finding studies (e.g., LD50 determinations, skin/eye irritation tests, etc.). In its response, the Agency stated that "many routine tests are based on knowledge of toxicity associated with a chemical...." EPA's response also directed that unknown effects that occur and are observed/determined during such routine studies may have to be reported to EPA under Section 8(e) if such effects are serious and meet the reporting requirements set forth in the Section 8(e) policy statement. Thus, when evaluating the results of acute animal toxicity studies for possible submission to EPA under Section 8(e) of TSCA, EPA believes that subject companies should consider such factors as the lethal dose, the pH of the tested chemical or mixture, the route of administration, the occurrence of unexpected effects (which could be determined via "cage-side" observation or during necropsy), and the extent and pattern of the actual or potential exposure to the tested chemical or mixture. In general, when evaluating such information for TSCA Section 8(e) reporting, the greater the acute toxicity, the less heavily a subject company should weigh the exposure to the tested chemical or mixture, and vice versa.

In light of the preceeding discussion, it does not appear that the acute toxicity information, as presented in this submission, warranted reporting to EPA under Section 8(e) of TSCA. In making this initial determination, however, it should be understood that the Agency may not be aware of additional pertinent information that may have been available to and/or considered by the submitting company in deciding to report under Section 8(e).

a) The Chemical Screening Branch will request the submitter to provide to EPA a complete copy of the final report (including experimental protocol and data) from each toxicity study that was cited in the submission. In addition, the submitter will be asked to report the exact structure (if known) and pH (if known) of the tested material. Finally, the submitting company will be requested to provide its rationale (in light of the discussion presented in the Comments/Recommendations section of this report) as to why the acute in vivo toxicity information is believed to have warranted submission to EPA under Section 8(e) of TSCA.

Considering EPA's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the submitting company will be asked to describe the actions it has taken or plans to take to (1) warn workers and others, and (2) reduce and/or eliminate exposure to the tested chemical. The submitting company will be asked also to describe the nature of all other tests that it has conducted, is conducting, or plans to conduct that are designed to determine the toxicity of and/or the exposure to the chemical.

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of the subject chemical substance.

c) The Chemical Screening Branch will send a copy of this status report to NIOSH, OSHA, CPSC, OW/EPA, OSWER/EPA, OAR/EPA, and ORD/EPA. Copies of this status report will be sent also to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: OCT 25 1984

SUBJECT: Status Report* 8EHQ-1084-0532

FROM: David R. Williams, DRW Acting Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Approved 10/29/84

Revision Needed ______

Submission Description

The Allied Corporation provided the following summarized results from several toxicologic studies of 5,7,11-dodecatriyn-1-ol:

"Dermal Irritation - moderately irritating.

Sensitization (maximization test) - extreme sensitizer. [A Section] 8(c) notification was also recorded which indicated a possible dermal irritation and sensitization in a laboratory technician.

Photosensitization (guinea pig) - negative. NOTE: Histopathological examination showed a brain lesion in each of two animals observed to have neuromuscular effects.

Cross-sensitization - may induce the potential for cross-sensitization by other compounds or will react as an intermediate sensitizer where animals have been induced with other sensitizing substances.

Mutagenicity - negative [in vitro] Ames [bacteria] test.

Acute Oral Toxicity (rats) - LD50 appears to be <0.3 ml/kg. Pathological examination suggests the development of brain lesions similar to those observed in guinea pigs (noted for photosensitization).

Subacute Probe Oral Toxicity (rats) - non-pregnant rats were dosed for 21 days. Neurobehavioral screens indicated balance problems and weakness of fore and hind legs.

Fetotoxicity Study - no maternal toxicity after dosing for 5 days premating and 15 days into gestation. However, there may be a statistically significant difference in litter size and weight when comparing the high dose and controls. Other aspects of this study (just now being completed) are still under evaluation."

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Submission Evaluation

The submitted information indicates that 5,7,11-dodecatriyn-1-ol and/or its metabolite(s) can be absorbed following either dermal application or oral administration. The information also indicates that the chemical and/or its metabolite(s) possess neurotoxic, sensitizing, and potential fetotoxic activities. Further evaluation of the reported findings should be possible upon the Agency's receipt of a full copy of the final report (including the actual experimental protocol and data) from each study that was cited in the submission.

It should be noted also that there is some degree of structural analogy between 5,7,11-dodecatriyn-1-ol and 1-hexyn-3-ol. The latter chemical was the subject of a previous TSCA Section 8(e) notice (8EHQ-0179-0273) which was submitted by the Dow Chemical Company). In its Section 8(e) notice, Dow reported that 1-hexyn-3-ol had been shown to be toxic to laboratory animals via dermal, oral, and inhalation routes of exposure and caused the death of an employee (of a former Dow subsidiary) following an accidental single dermal exposure to "a large amount" of the chemical.

Current Production and Use

According to Allied, all of its work to date with 5,7,11-dodecatriyn-1-ol has been research and development (R&D) related. The company stated in its submission that the projected commercial use of the subject chemical "is as an intermediate which though it would be isolated would also be in a closed system, a fact limiting exposure potential." Allied also reported, however, that the company is "not sure at this time that this material will be commercialized." Finally, the Allied Corporation stated that approximately 1 kg of the chemical has been synthesized to date and that "exposure has been limited to laboratory personnel at Allied and two other contract laboratories."

Comments/Recommendations

In its submission, Allied reported that all personnel working with 5,7,11-dodecatriyn-1-ol have been notified about the submitted toxicologic findings.

On August 22, 1983, the Agency published (48 FR 38178) a final rule that required full compliance with Section 8(c) of TSCA as of November 21, 1983. In general, the final 8(c) rule requires chemical manufacturers/importers and certain processors to maintain records of significant adverse reactions to health or the environment alleged to have been caused by chemical substances or mixtures. The final Section 8(c) rule also requires that allegations involving significant adverse reactions in employees be maintained for 30 years and that all other allegations be maintained for 5 years. It should be noted that although there is no automatic Section 8(c) record-reporting requirement in place at the present time, EPA can inspect and/or require the submission of TSCA Section 8(c) records to the Agency.

a) The Chemical Screening Branch (CSB/ECAD/OTS) will ask the Allied Corporation to provide to EPA a complete copy of the TSCA Section 8(c) allegation/report and the final report (including the actual experimental protocol and data) from each toxicity study that was cited in Allied's submission. In view of the Agency's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the Chemical Screening Branch will also request Allied to describe the nature of all other studies that the company has conducted, is conducting, or is planning to conduct that are designed to define the toxicity of and/or the exposure to 5,7,11-dodecatriyn-1-ol.

b) In light of the structural analogy between 1-hexyn-3-ol and 5,7,11-dodecatriyn-1-ol, the Chemical Screening Branch will request the Dow Chemical Company to describe the nature of all studies (with the exception of those reported by the company in 8EHQ-0179-0273) that Dow has conducted, is conducting, or plans to conduct that are designed to determine the toxicity of and/or the exposure to 1-hexyn-3-ol. In addition, Dow will be asked if the company has recorded any TSCA Section 8(c) allegations concerning 1-hexyn-3-ol, and if so, how many.

The Chemical Screening Branch will review the reported information to determine the need for further OTS assessment of 5,7,11-dodecatriyn-1-ol and/or 1-hexyn-3-ol.

d) The Chemical Screening Branch will transmit copies of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OSWER/EPA, OW/EPA, OAR/EPA and ORD/EPA. In addition, copies of this status report will be sent to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-1084-0533 S
Page 1 of 3

DATE: OCT 25 1984

SUBJECT: Status Report* 8EHQ-1084-0533 S

Approved 10/30/84

FROM: David R. Williams, DRW Acting Section Head
Chemical Risk Identification Section/CSB

Revision Needed ______

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Note: The submitting company has claimed its name as TSCA Confidential Business Information (TSCA CBI). The Information Management Division (IMD/OTS/OPTS) has requested the submitting company to substantiate its confidentiality claim.

Submission Description

The submitting company provided summarized results from several genotoxicity studies of 2-chloro-5-trichloromethyl pyridine (CAS No. 69045-78-9). According to the submitter:

> "A preliminary Ames test in Salmonella strain TA 98 with a metabolic activation system (S9), gave a negative result. Recently further tests were conducted with five Salmonella strains, with and without S9, and a positive result was obtained in TA 98 without activation. Subsequently positive results were obtained in a mouse lymphoma assay and an in vitro human lymphocyte cytogenetic assay.
>
> "Our [the submitter's] laboratory concludes that 2-chloro-5-trichloromethyl pyridine is mutagenic to bacteria under certain conditions and should be considered potentially mutagenic to higher animals and man."

Submission Evaluation

Although the submitted information does indicate that 2-chloro-5-trichloromethyl pyridine possesses some degree of genotoxic activity, complete copies of the final reports (including the actual experimental protocols and data) from all of the cited studies are needed in order for the Agency to evaluate the reported findings.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Current Production and Use

The subject chemical was not located during a review of the non-confidential portion of the TSCA Inventory. The submitting company reported that it "does not currently manufacture, distribute or process ...[2-chloro-5-trichloromethyl pyridine]...." and "that to our [the company's] knowledge, this material has been used only as an industrial intermediate under conditions that ensure minimal exposure, whether by inhalation or skin contact." According to a publicly available on-line computerized data base (Toxline), 2-chloro-5-trichloromethyl pyridine is associated with a patent (Eur. Pat. Appl. (Patent No. 4414) 10/03/79) concerning the synthesis and uses of herbicides.

Comments/Recommendations

Although a positive genotoxicity test result, when considered alone, may not be sufficient to offer reasonable support for a conclusion of substantial risk, the Agency believes that such results are of value in assessing the possible risks posed by chemicals to health and/or the environment. EPA also believes that positive genotoxicity test results in combination with additional information (e.g., knowledge of potential exposure to or high production of the chemical substance or mixture), would suggest, in many cases, the need to conduct additional studies designed to define better the toxicity of and/or exposure to the chemical substance or mixture. The results of such studies should be considered also for possible submission to the Agency under Section 8(e) of TSCA.

It should be noted that EPA's Office of Toxic Substances (OTS) has received and evaluated several TSCA Section 8(e) notices containing toxicologic and/or exposure information on a number of substituted pyridines. In addition, the Chemical Screening Branch (CSB/ECAD/OTS) has prepared Chemical Hazard Information Profiles (CHIPs) on 2-, 3-, and 4-methyl pyridine and staff of the Risk Management Branch (RMB/ECAD/OTS) is currently evaluating the available toxicity/exposure information on these chemicals. It should be noted also that EPA has received and evaluated a number of TSCA Section 5 Premanufacturing Notifications (PMNs) for substituted pyridines.

a) The Chemical Screening Branch will ask the submitter to ensure that EPA receives a complete copy of the final report (including the actual test protocol and data) from each genotoxicity study that was cited in the submission.

   In view of EPA's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the Chemical Screening Branch will request the submitting company to describe all other studies that it has conducted, is conducting, or plans to conduct to define the toxicity of and/or the exposure to 2-chloro-5-trichloromethyl pyridine.

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of 2-chloro-5-trichloromethyl pyridine.

c) The Chemical Screening Branch will send a copy of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OSWER/EPA, OW/EPA, ORD/EPA, OAR/EPA, OPP/OPTS, and CCD/OTS/EPA. In addition, copies of this status report will be provided to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-1084-0534
Page 1 of 3

DATE: NOV 7 1984

SUBJECT: Status Report* 8EHQ-1084-0534

Approved 11/07/84

Revision
Needed

FROM: David R. Williams, DRW Acting Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The Tennessee Eastman Company provided the following summarized results from a sub-acute oral toxicity study of 2-methoxyethyl palmitate (2-MEP; CAS No. 111-07-9) in rats:

> "Groups of 5 male rats were treated with either 100 or 1000 mg/kg of 2-methoxyethyl palmitate by gavage 11 times over 15 days. The primary effect was observed on the testes. All high dose animals showed small, soft testes with severe bilateral atrophy of testicular epithelium and degenerations of spermatids; multinucleated spermatid formation was observed in 2 of 5 animals, while 3 of 5 animals showed reduced amounts of seminal fluid in the seminal vesicles. In low dose animals, 2 of 5 showed minimal bilateral atrophy of testicular epithelium with degeneration of spermatids and minor to moderate reduction of spermatozoa in the epididymal lumena."

Submission Evaluation

The submitted information indicates that 2-methoxyethyl palmitate (2-MEP) causes dose-related adverse testicular effects in rats after 11 oral exposures (over 15 days) at levels of 100 mg/kg/day and 1000 mg/kg/day. The observed testicular effects were most likely caused by 2-methoxyethanol (2-ME), a suspected in vivo metabolite of 2-MEP. Other esters of 2-ME, such as 2-ME acetate and 2-ME phthalate, produce the same toxicity profile as 2-ME, a chemical that has been shown to cause adverse testicular and developmental effects in several species via oral, dermal and inhalation exposure.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Current Production and Use

A review of the production range (includes importation volumes) statistics for 2-methoxyethyl palmitate (CAS No. 111-07-9), which is listed in the initial TSCA Inventory, has shown that between 1 million and 10 million pounds of this chemical were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed as TSCA Confidential Business Information (TSCA CBI) by the person(s) reporting for the TSCA Inventory, nor does it include any information which would compromise TSCA CBI. The data submitted for the TSCA Inventory, including the production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

The submitter provided the following information with regard to the current production and uses of and the potential for exposure to 2-MEP:

> "2-MEP is manufactured and used by Tennessee Eastman Company. Total annual production is less than 1 million kg. The primary use is as a plasticizer for cellulosic plastics. A secondary use is as a minor component in a fiber lubricant. The majority of manufacturing and processing operatons for 2-MEP are enclosed or are controlled release processes. Employee exposure is limited by the use of personal protective equipment, local or building ventilation, and by the very low volatility (boiling point of 310°C) of the chemical."

Comments/Recommendations

In its submission, the Tennessee Eastman Company reported that the current handling procedures and precautionary information for 2-methoxyethyl palmitate will be updated to reflect the reported toxicologic findings. The company also reported that, upon completion, a final report of the 15-day toxicity study will be sent to the Agency.

EPA's Office of Toxic Substances (OTS) has received and evaluated a number of TSCA Section 8(e) and "For Your Information" (FYI) submissions containing toxicologic and/or exposure information on glycol ethers including: 2-methoxyethanol (and its acetate), 2-ethoxyethanol (and its acetate), and 2-butoxyethanol. In addition, the Chemical Screening Branch (CSB/ECAD/OTS) has prepared Chemical Hazard Information Profiles (CHIPs) on 2-methoxyethanol and its acetate and 2-ethoxyethanol and its acetate. It should be noted also that the Risk Management Branch (RMB/ECAD/OTS) is currently evaluating available toxicologic and exposure data on a number of glycol ethers. Finally, the Test Rule Development Branch (TRDB/ECAD/OTS) is currently evaluating available toxicologic and exposure data on 2-phenoxyethanol, a chemical that was recommended by the Interagency Testing Committee (ITC) for testing consideration by EPA under Section 4 of TSCA.

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will request the Tennessee Eastman Company to ensure that EPA receives a complete copy of the final report (including the actual experimental protocol and data) from the 15-day rat toxicity study of 2-MEP that was cited in the company's submission.

In light of the Agency's general interest in corporate actions that are taken on a voluntary basis in response to chemical toxicity and/or exposure information, the Chemical Screening Branch will ask the Tennessee Eastman Company to describe the nature of all other studies that the company has conducted, is conducting, or is planning to conduct to define the toxicity of and/or the exposure to 2-methoxyethyl palmitate.

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of 2-methoxyethyl palmitate.

c) The Chemical Screening Branch will send copies of this status report to OSHA, NIOSH, CPSC, FDA, NTP, OSWER/EPA, OW/EPA, ORD/EPA, OAR/EPA, and RMB and TRDB/ECAD/OTS. In addition, copies of this report will be sent to the TSCA Assistance Office (TAO/OTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-1084-0535
Page 1 of 6

DATE: NOV 20 1984

SUBJECT: Status Report* 8EHQ-1084-0535

Approved 11/21

Revision Needed ______

FROM: David R. Williams DRW Acting Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The 3M Company reported that the results of several recently conducted acute inhalation toxicity studies in rats and quail indicate that mixtures of 1,1,1-trichloroethane (TCE) and perfluoroalkyl resins are more toxic than 1,1,1-trichloroethane alone. The submitter also reported that the provided information is considered new in that "it was previously believed, based on past studies, that the acute toxicity and hazard of the mixture was the same as the acute toxicity and hazard of the [TCE] solvent." The 3M Company provided the following compositional information for the tested mixtures:

T-3500	0.5%	Perfluoroalkyl Resin (CAS No. 68298-78-2)
	.03%	Stearamide Solid (CAS No. 10212-58-5)
	0.3%	Freon 113 (CAS No. 76-13-1)
	0.3%	Methyl Isobutyl Ketone (CAS No. 108-10-1)
	99%	1,1,1-Trichloroethane (CAS No. 71-55-6)
T-3499	10%	Perfluoroalkyl Resin (CAS No. 68555-92-0)
	90%	1,1,1-Trichloroethane (CAS No. 71-55-6)

The 3M Company provided the following information regarding the conduct and results of the performed acute toxicity studies as well as two studies designed to define human exposure to products containing T-3500.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

"Protocol: The inhalation exposures were for 4 hours in a one cubic meter chamber. Animals were suspended in individual cages in the middle of the chamber. Ten rats and ten quail (five males, five females per species) were exposed. Airflow was approximately 180 l/minute with a temperature of [approx.] 72°F and relative humidity [of approx.] 50%. The solutions were injected into the air stream by a syringe pump through a 1/4" J-nozzle nebulizer at the top of the chamber. TCE levels were measured using a MIRAN analyzer. Resin levels were measured by chemical analysis of glass fiber filters. Particle size was measured using a TSI particle size analyzer.

"Results: The LC50s for TCE [alone] were determined to be about 14,000 ppm for both rats and quail. The TCE LC50 (rat) is comparable to that in the literature. T-3500 was initially run at the LC50 for the solvent and then at progressively lower levels. The LC50 (rat) was determined to be 170 ppm TCE (with [approx.] 2 mg resin/m^3). Particle size data indicate approximately 95% of the particles to be in the respirable range. Preliminary gross pathology indicates death to be the result of pulmonary effects rather than CNS depression or cardiac sensitization which are known causes of toxicity in TCE exposures. In quail, the LC50 is less than 14 ppm TCE (0.25 mg resin/m^3). Further runs to determine the LC50 for quail were abandoned due to problems in delivering so little material over a four hour period. A trial run of T-3499 showed the resin content (10%) to cause delivery problems by clogging the nebulizer. A 10-fold dilution of T-3499 with TCE was run at 1910 ppm TCE (66 mg resin/m^3) resulting in the death of all rats and quail.

"Additional Animal Study Results: LC50s for rats of 1:30 and 1:60 dilutions of T-3500 to TCE were determined. The 1:30 dilution had 0.0167% solids and the 1:60 dilution had 0.0083% solids. The LC50s are about 1500 ppm TCE (0.34 mg resin/m^3) and 1450 ppm TCE (Resin levels have not yet been determined.), respectively.

"The toxicity data indicate that under the condition of the experiments:

1. The TCE/perfluoroalkyl resin solutions are extremely toxic to quail.
2. The mixtures are more toxic to rats than the solvent alone.
3. T-3500 dilutions are less toxic than T-3500 but are more toxic than the solvent alone."

"Human Exposure Study: Since T-3500, when sprayed directly into the chamber, was more toxic than expected, simulated applications were run to determine if users of spray products containing T-3500 could be at risk. During use, the product is sprayed away from the user's breathing zone on to a substrate. Most of the resin is deposited onto the cloth. Therefore, the actual resin level that the user is exposed to is less than that sprayed directly into the chamber.

"As an exaggerated use condition, four 16 oz. containers of T-3500 were sprayed sequentially onto 10 square yards of cloth in an unventilated room. Operator breathing zone levels of TCE ranged from 563 ppm after spraying one container to 1650 ppm after four [containers]. The analysis of resin levels varied inconsistently. Levels ranged from 0.008 to 0.130 mg/m^3. (This may indicate an analytical or contamination problem.) Particle size was not determined. There appears to be an estimated 30 to 60 fold reduction in resin levels in the applicator's breathing zone as compared to the measured resin values in the animal inhalation studies.

"Additional Human Exposure Study: Air sampling was conducted during the spraying of a sofa in a room following the instructions on the 16 oz. product. Three cans were used. Maximum TCE levels in the operator breathing zone were achieved after spraying one can (136 ppm). TCE levels averaged 34 ppm over the time period for spraying 3 cans. Again, resin values varied inconsistently (nondetectable to 0.095 mg/m^3). Resin particle size was not determined.

"The air sampling data indicate that in simulated use:

1. TCE levels vary widely depending on the amount of aerosol sprayed and the degree of ventilation in the room.

2. Perfluoroalkyl resin levels are not yet reliably known."

Current Production and Use

The 3M Company provided the following information concerning the uses of commercial products containing TCE and perfluoroalkyl resins.

> "Perfluoroalkyl resins are constituents of some stain repellent products. Numerous stain repellent products are sold by 3M and other manufacturers. Most are sold as water emulsions for application by fabric mills and would not be included in the consideration of this [TSCA Section] 8(e) submittal. 3M does sell five products that contain 1,1,1-trichloroethane solutions of perfluoroalkyl resins: two of these products are sold as high solids industrial products for use by textile finishers; and one is a ready-to-use

formulation applied by the retailer as an airless spray, under controlled conditions, to upholstered furniture. A fourth product is sold as an industrial product used by leather finishers and to a smaller extent as a concentrate for formulation in an aerosol stain repellent sold by retail outlets. ...[3M] believe[s] the manufacture of these products, and their use by industrial customers or licensed retailers, does not present a risk to workers because the recommended industrial hygiene procedures and precautions preclude significant exposure to the mixtures.

"The fifth product is an aerosol stain repellent sold by retail outlets. During the past two decades tens of millions of units have been sold. Given this broad consumer experience with the product, the numbers of adverse health complaints have been low. Pulmonary complaints have numbered about 25 since 1965. There have been no known deaths from the use of the product under normal or misuse conditions. There have been 7 known deaths in the U.S. due to intentional abuse, i.e., deliberately inhaling spray from a bag, (4 teenage males, 1 male and 1 female in their 20's, and 1 unknown).

"The toxicity and simulated use air sampling data indicate aerosol usage of a TCE/perfluoroalkyl resin mixture may present a greater hazard than was previously thought. However, the 20 years of customer history would indicate the risk (the probability of the hazard occurring) is quite low. The reasons for this may be attributable to:

1. Time of exposure. It takes about 6 minutes to spray a 16 oz. container which is enough to cover 20-50 square feet of cloth. The toxicity studies are based on exposures where the material is being continuously sprayed into the test chamber for 4 hours.

2. Ratio of the Mixture. The aerosol product is intended to deposit the resin directly onto the material. The actual amount of resin available for inhalation with solvent is extremely low.

3. Labelling. The current aerosol product label instructs the user to provide adequate ventilation, including fans and open windows or to use outdoors if possible. [The label] warns against using in small rooms, bathrooms, or closets, that intentional misuse or use in a poorly ventilated or closed area may be harmful or fatal and that small children and pets should be kept out of the area until treated substrate is dry."

Submission Evaluation

The submitting company compared the LC50 for 1,1,1-trichloroethane (TCE) aerosol propellant (which was determined to be approximately 14,000 ppm for both rats and quail) with the LC50 for a mixture containing 99% 1,1,1-trichloroethane and 0.5% perfluoroalkyl resin, plus additional organic compounds including 0.3% methyl isobutyl ketone. The LC50 was dramatically reduced in the 4-hour inhalation tests on the mixture: 170 ppm TCE (with approximately 2 mg of resin per cubic meter of air) in the rat and 14 ppm TCE (with approximately 2 mg of resin per cubic meter of air) in the quail. Death was attributed by the testing laboratory to unspecified "pulmonary effects rather than CNS depression or cardiac sensitization," based on preliminary gross pathology findings. Approximately 95% of the resin particles were of respirable size. It may be misleading to speak of the LC50 in terms of units (ppm) of TCE. The experiment does not establish (nor rule out) that a synergistic reduction in the LC50 for TCE has occurred; TCE may have been no more than an inert carrier that was measured for convenience, assuming a reasonably homogenous mixture, with toxicity being attributable to the resin. If the toxicity is in fact due chiefly or exclusively to the resin, then this submission is an instructive exception to general expectations that polymers are inherently non-toxic.

The final reports (including protocols and experimental data) from all of the cited studies should be requested by EPA in order to evaluate more fully the reported toxicologic findings. In particular, it would be useful to know the nature of the observed "pulmonary effects." It would also be useful to know whether the perfluoroalkyl resins decompose to yield toxic products, and under what conditions such decomposition can occur.

The submission does not make clear whether the tested substances have been used in marketed products for either professional or consumer use. Although it is inviting to reason that the potential human hazard is probably minimal (because great numbers of aerosol cans have been used without serious harm), this conclusion may be untenable if the experience with human exposures has involved different resins, or if cases of toxicity have occurred but have gone unrecognized or unreported.

Comments/Recommendations

According to 3M, additional inhalation studies are underway and aerosol product labels are being revised in order to place greater emphasis upon the precautions to be observed during use. In addition, 3M reported that the Consumer Product Safety Commission (CPSC) and foreign governments were being notified about the findings presented in the company's TSCA Section 8(e) submission.

EPA's Office of Toxic Substances (OTS) has received and evaluated a number of TSCA Section 8(e) and "For Your Information" (FYI) submissions containing toxicologic and/or exposure information on methyl isobutyl ketone, 1,1,1-trichloroethane and perfluoroalkyl compounds. It should also be noted that the Risk Management Branch (RMB/ECAD/OTS) is currently evaluating available toxicologic and exposure data on a number of perfluoroalkyl compounds.

Finally, the Test Rule Development Branch (TRDB/ECAD/OTS) is currently evaluating available toxicologic and exposure data on 1,1,1-trichlorethane and methyl isobutyl ketone, chemicals that were recommended by the Interagency Testing Committee (ITC) for testing consideration by EPA under Section 4 of TSCA.

a) The Chemical Screening Branch (CSB/ECAD/OTS/OPTS) will request the 3M Company to ensure that EPA receives a complete copy of the final report (including the actual experimental protocol and data) from each of the toxicity and human exposure studies that were cited in the company's submission.

In light of the Agency's general interest in corporate actions that are taken on a voluntary basis in response to chemical toxicity and/or exposure information, the Chemical Screening Branch will ask the 3M Company to describe the nature of all other studies that the company has conducted, is conducting, or is planning to conduct to define the toxicity of and/or the exposure to TCE/perfluoroalkyl resin mixtures. In addition, 3M will be asked to describe the actions the company has taken to notify 3M workers about the reported findings. Finally, 3M will be asked if the company's revised product label will include further more explicit wording with regard to potential serious health effects.

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of the subject chemicals.

c) The Chemical Screening Branch will send copies of this status report to OSHA, NIOSH, CPSC, FDA, NTP, OSWER/EPA, OW/EPA, ORD/EPA, OAR/EPA, and RMB and TRDB/ECAD/OTS. In addition, copies of this report will be sent to the TSCA Assistance Office (TAO/OTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-1184-0536
Page 1 of 3

DATE: DEC 17 1984

SUBJECT: Status Report* 8EHQ-1184-0536

Approved 12/17/84

FROM: David R. Williams DRW Acting Section Head
Chemical Risk Identification Section/CSB

Revision Needed ________

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The Gulf Oil Products Company provided the following summarized information concerning the results of two genotoxicity tests conducted with cumene ((1-methylethyl)benzene; CAS No. 98-82-8):

> "In the Cell Transformation Test, BALB/3T3 mouse embryo cells were exposed to cumene while growing in tissue culture. Positive and vehicle controls were run simultaneously. Transformation was observed at 60 mcg/ml. The test was considered positive.
>
> "In the second test, the Hepatocyte Primary Culture/DNA Repair Test, primary hepatocytes from Fisher 344 rats were exposed to cumene while growing in tissue culture. The ability of the cells to take up radioactive thymidine during the exposure period was measured. Positive and vehicle controls were run simultaneously. Unscheduled DNA synthesis was observed at 16 mcg/ml. This test was considered positive for cumene."

In its submission, the Gulf Oil Products Company reported also that a "Mammalian Cell Point Mutation Test (CHO) and a Chromosome Aberration (Micronucleus) Test are in progress at the Gulf Life Sciences Laboratory," but "no information on the outcome of these tests [is available] at this time."

Submission Evaluation

Although the submitted information indicates that cumene does possess some degree of genotoxic activity, a full copy of the final report (including the actual experimental protocol and data) from each study that was cited in the submission is needed in order for EPA to evaluate the significance of the reported findings. Immediately upon receipt of this submission, a copy was provided to the Test Rules Development Branch (TRDB/ECAD/OTS) for inclusion in their review of available toxicologic/exposure information on cumene, a chemical recently recommended by the Interagency Testing Committee (ITC) for testing under Section 4 of TSCA.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Current Production and Use

A review of the production range (includes importation volumes) statistics for cumene (CAS No. 98-82-8), which is listed in the initial TSCA Inventory, has shown that over 2.5 billion pounds of this chemical were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed as TSCA Confidential Business Information (TSCA CBI) by the person(s) reporting for the TSCA Inventory, nor does it include any information that would compromise TSCA CBI. The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

The May 7, 1984 issue of Chemical & Engineering News estimates that the annual cumene production was 2.74 and 3.30 billion pounds in 1982 and 1983, respectively.

According to secondary literature sources, cumene is used 1) in the production of phenol and acetone (major uses), acetophenone, alpha-methylstyrene, oxidation catalysts, and peroxides; 2) as an aviation fuel additive; and 3) as a solvent.

Comments/Recommendations

In its submission, the Gulf Oil Products Company stated that the company plans to conduct a thorough review of its cumene handling procedures and "intends to review the Material Safety Data Sheet (MSDS) and the label for ...[cumene] to be sure they delineate the toxic properties of this material and adequately warn workers and customers about procedures for safe handling...." The submitter also stated that "if there is any change in the MSDS, Gulf will mail the revised form along with an explanatory letter to all customers of record." Finally, the submitter stated that, upon completion, copies of the final genotoxicity study reports would be transmitted to the Agency.

Although a positive genotoxicity test result, when considered alone, may not be sufficient to offer reasonable support for a conclusion of substantial risk, the Agency believes that such results are of value in assessing the possible risks posed by chemicals to health and/or the environment. EPA also believes that positive genotoxicity test results in combination with additional information (e.g., knowledge of potential exposure to or high production of the chemical substance or mixture), would suggest, in many cases, the need to conduct additional studies designed to define better the toxicity of and/or exposure to the subject chemical substance or mixture. The results of such studies should be considered also for possible submission to the Agency under Section 8(e) of TSCA.

On November 28, 1984, EPA published TSCA Section 8(a) and 8(d) reporting rules (49 FR 46739 and 49 FR 46741, respectively) for cumene. It should be noted also that the Chemical Screening Branch (CSB/ECAD/OTS) has prepared a Chemical Hazard Information Profile (CHIP) on cumene hydroperoxide, a chemical intermediate in the cumene-phenol/acetone production process.

(a) The Chemical Screening Branch (CSB/ECAD/OTS) will request the Gulf Oil Products Company to ensure that EPA receives, when completed, a full copy of the final report (including the actual experimental protocol and data) from each genotoxicity study cited in the submission. Immediately upon receipt of the requested reports, the Chemical Screening Branch will provide copies to the Test Rules Development Branch/ECAD for inclusion in their review of cumene under Section 4 of TSCA.

(b) The Chemical Screening Branch will send a copy of this status report to NIOSH, OSHA, CPSC, NTP, OW/EPA, OSWER/EPA, ORD/EPA, OAR/EPA, ORD/EPA, and TRDB/ECAD/OTS. In addition, copies of this status report will be sent to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-1184-0537
Page 1 of 3

DATE: DEC 17 1984

SUBJECT: Status Report* 8EHQ-1184-0537

FROM: David R. Williams, Acting Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Approved 12/17/84

Revision Needed ________

Submission Description

The Gulf Oil Products Company provided the following summarized information with regard to the results of several genotoxicity studies conducted with Gulf's Light Pyrolysis Fuel Oil:

> "Light Pyrolysis Fuel Oil was tested for the ability to damage DNA in the primary rat hepatocytes growing in tissue culture by using autoradiography to measure the ability of the cells to incorporate radioactive thymidine. Vehicle and positive control groups were run simultaneously. Unscheduled DNA Synthesis was observed at 8 mcg/ml. The Study Director concluded that the test was positive for genetic damage.
>
> "Three other genetics tests have been performed on this product. A Mammalian Cell Point Mutation Test was negative for point mutations. The material had no effect on the frequency of micronucleated erythrocytes in the bone marrow, i.e., the Micronucleus Test was negative. In a Cell Transformation Test in BALB/3T3 Mouse Embryo Cells, transformation was not observed at any level of Light Pyrolysis Fuel Oil dosing."

Submission Evaluation

Although the submitted information indicates that Gulf's Light Pyrolysis Fuel Oil does possess some degree of genotoxic activity, a complete copy of the final report (including the actual experimental protocol and data) from each study cited in the submission is needed in order for the Agency to evaluate the significance of the reported findings.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Current Production and Use

Although no Chemical Abstract Service (CAS) Number was located for Light Pyrolysis Fuel Oil, the TSCA Inventory (Appendix A) defines pyrolysis fuel oil as follows:

> "The complex combination of hydrocarbons obtained from the initial water quenching of the effluent gases from a thermal cracking of ethane, propane or light naphtha. This stream is likely to contain 5 wt. % or more of 4- to 6- membered condensed ring aromatic hydrocarbons."

A review of the production range (includes importation volumes) statistics for pyrolysis fuel oil (CAS No. 69013-21-4), which is listed in the initial TSCA Inventory, has shown that no 1977 production/importation was reported or that all of the production range data reported were claimed as TSCA Confidential Business Information (TSCA CBI) by the manufacturer(s) and/or importer(s) and cannot be disclosed (Section 14(a) of TSCA, U.S.C. 2613 (a)). The data submitted for the TSCA Inventory including production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

The Gulf Oil Products Company did not provide any information with regard to the current production or specific use(s) of its Light Pyrolysis Fuel Oil nor was such information located in the secondary literature sources consulted.

Comments/Recommendations

In its submission, the Gulf Oil Products Company reported that it "intends to review the Material Safety Data Sheet and the label for ...[Gulf's Light Pyrolysis Fuel Oil] product to be sure they adequately reflect the toxicity data available and that the protective practices recommended are adequate to protect both Gulf workers and customers." The submitter also reported that "if there is any change in the MSDS, Gulf will mail the revised form with an explanatory letter to all customers of record." Finally, the Gulf Oil Products Company stated that copies of the final genoxicity study reports (upon completion) would be sent to EPA.

Although a positive genotoxicity test result, when considered alone, may not be sufficient to offer reasonable support for a conclusion of substantial risk, the Agency believes that such results are of value in assessing the possible risks posed by chemicals to health and/or the environment. EPA also believes that positive genotoxicity test results in combination with additional information (e.g., knowledge of potential exposure to or high production of the chemical substance or mixture), would suggest, in many cases, the need to conduct further studies designed to define better the toxicity of and/or exposure to the chemical substance or mixture. The results of such further studies should be considered also for possible submission to the Agency under Section 8(e) of TSCA.

EPA's Office of Toxic Substances (OTS) has received and evaluated a number of TSCA Section 8(e) and "For Your Information" submissions containing toxicologic and/or exposure data on a variety of coal, shale, and petroleum oils, process streams, and/or wastes.

(a) The Chemical Screening Branch (CSB/ECAD/OTS) will request the Gulf Oil Products Company to ensure that EPA receives, when completed, a full copy of the final report (including the actual experimental protocol and data) from each genotoxicity study that was cited in the company's submission.

In view of EPA's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the Chemical Screening Branch will request the submitting company to describe all other studies that it has conducted, is conducting, or plans to conduct to define the toxicity of and/or the exposure to Gulf's Light Pyrolysis Fuel Oil.

(b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of Light Pyrolysis Fuel Oil.

(c) The Chemical Screening Branch will send a copy of this status report to NIOSH, OSHA, DOE, CPSC, NTP, OW/EPA, OSWER/EPA, OAR/EPA and ORD/EPA. Copies of the status report will also be provided to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-1284-0538
Page 1 of 2

DATE: DEC 20 1984

SUBJECT: Status Report* 8EHQ-1284-0538

FROM: David R. Williams, drw Acting Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Approved 12/21/84

Revision Needed ____________

Submission Description

Air Products and Chemicals, Inc. provided the following summary with regard to the interim results of an ongoing 2-year inhalation study of Solvent-Refined Coal (SRC) Solid "dust" in rats. According to the company,

> "An intermediate (12 months) sacrifice has been performed, and the preliminary results obtained indicate occurrence of tumors in only the females of the highest exposure group (50 mg/m^3). They have been initially described as keratinizing squamous epithelioma (a potentially malignant tumor). Pathological evaluation of tissues from the lower exposure groups is being undertaken. This inhalation study will continue for another year after which time more complete data will be available."

In its submission, Air Products and Chemicals, Inc. reported that this study is being conducted by the company under contract for the U.S. Department of Energy (DOE). In addition, the company noted that "two [Section] 8(e) Notices previously submitted ...by the International Coal Refining Company [8EHQ-0683-0482 and 8EHQ-1283-0482 Followup] reported positive results in an Ames Test and Mouse Lymphoma Test using [a] DMSO extract of the SRC Solid and on other portions of SRC-I solids. Those previous [Section] 8(e) notices are related to the present one."

Submission Evaluation

Although the reported interim findings do indicate that SRC Solid dust possesses some degree of oncogenic activity in female rats, complete copies of future interim reports and the final report (including the experimental protocol and data) from the 2-year inhalation study are needed in order for the Agency to evaluate the significance of the findings.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Current Production and Use

Although Air Products and Chemicals, Inc. did not provide any information concerning current production or use(s) of the subject SRC material, the International Coal Refining Company did report (in the previously cited Section 8(e) submissions) that the "current use of SRC-I materials, in addition to being carefully controlled, is limited to research and testing purposes at a limited number of research and testing facilities." It should be noted also that a number of SRC materials are listed in the initial TSCA Chemical Substances Inventory.

Comments/Recommendations

EPA's Office of Toxic Substances (OTS) has received and evaluated a number of TSCA Section 8(e) and "For Your Information" (FYI) submissions containing toxicity/exposure information on a variety of coal, shale, and petroleum oil refinery products, streams, and/or waste materials.

(a) The Chemical Screening Branch (CSB/ECAD/OTS) will request Air Products and Chemicals, Inc. to provide complete copies of the experimental protocol, future interim reports, and final report (including all data) from the 2-year SRC Solid dust inhalation study that was cited in the submission.

In view of the Agency's general interest in company actions that are taken in response to chemical toxicity/exposure information, the Chemical Screening Branch will ask Air Products and Chemicals, Inc. to describe the actions it has taken to 1) warn workers and others, and 2) reduce and/or eliminate exposure to SRC Solid dust. In addition, the submitting company will be asked to describe the nature of all other studies that the company has conducted, is conducting, or plans to conduct to define the toxicity of and/or the exposure to SRC Solid dust.

(b) The Chemical Screening Branch will review the reported information to determine the need for further OTS assessment of SRC Solid dust.

(c) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, DOE, OW/EPA, OSWER/EPA, OAR/EPA and ORD/EPA. Copies will be provided also to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: DEC 27 1984

SUBJECT: Status Report* 8EHQ-1284-0539

Approved 12/27/84

Revision Needed ____________

FROM: David R. Williams DRW/ Acting Section Head
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Submission Description

The NOR-AM Chemical Company provided summarized results from a battery of in vitro genotoxicity assays of pyrogallol (1,2,3-benzenetriol; CAS No. 87-66-1). According to the submitter, pyrogallol was found to be positive in the presence and absence of exogenous metabolic activation in 1) an Ames Test (Salmonella typhimurium bacteria strains TA 100 and TA 1537); 2) a cultured Mouse Lymphoma Cell Assay; and 3) a Metaphase Chromosome Analysis of cultured human lymphocytes. The submitter reported that the positives obtained in the performed studies "were produced by concentrations which were at or close to toxic levels in each test system." The submitter also stated that these results are not completely unexpected in that "pyrogallol is structurally similar to the catechols which are mutagenic in in vitro test systems."

Submission Evaluation

Considering that the 1981-82 National Institute for Occupational Safety and Health (NIOSH) Registry of Toxic Effects of Chemical Substances (RTECS) cites a variety of in vitro and in vivo genotoxicity studies in which pyrogallol was found to be positive, the submitted information appears to provide additional evidence that pyrogallol is genotoxic. A full copy of the final report (including the actual experimental protocol and data) from each study cited in the submission is needed in order for the Agency to evaluate the significance of the reported findings.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Current Production and Use

A review of the production range (includes importation volumes) statistics for pyrogallol (CAS No. 87-66-1), which is listed in the initial TSCA Inventory, has shown that between 10 thousand and 101 thousand pounds were reported as produced/imported in 1977. This production range information does not include any production/importation data claimed as TSCA Confidential Business Information (CBI) by the person(s) reporting for the Inventory, nor does it include any information that would compromise TSCA CBI. All data submitted for the Inventory, including production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

According to secondary literature sources, pyrogallol is used as an intermediate in the manufacture of a variety of substances (e.g., dyes, inks), as an antioxidant in lubricant oils; as an analytical reagent; as a reducing agent; as an antibacterial in medicine; as an intermediate in drug synthesis; as a photographic process chemical; and as a component in cosmetics and hair dyes.

Comments/Recommendations

Although a positive in vitro genotoxicity test result, when considered alone, may not be sufficient to offer reasonable support for a conclusion of substantial risk, the Agency believes that such results are of value in assessing the possible risks posed by chemicals to health and/or the environment. EPA also believes that positive genotoxicity test results in combination with additional information (e.g., knowledge of potential exposure to or high production of the chemical substance or mixture), would suggest, in many cases, the need to conduct further studies designed to define better the toxicity of and/or exposure to the chemical substance or mixture. The results of such further studies should be considered also for possible submission under Section 8(e).

(a) The Chemical Screening Branch (CSB/ECAD/OTS) will request the NOR-AM Chemical Company to submit a full copy of the final report (including the actual experimental protocol and data) from each genotoxicity study that was cited in the company's submission.

In light of the Agency's general interest in corporate actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the Chemical Screening Branch will ask the NOR-AM Chemical Company to describe the actions the company has taken to 1) warn workers and others, and 2) reduce or eliminate exposure to pyrogallol. In addition, the NOR-AM Chemical Company will be asked to describe all other studies that the company has conducted, is conducting, or plans to conduct to define the toxicity of and/or the exposure to pyrogallol.

(b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of pyrogallol.

(c) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, FDA, CPSC, NTP, OSWER/EPA, OW/EPA, OAR/EPA, ORD/EPA, and OPP/OPTS. In addition, copies of this report will sent to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: JAN 23 1985

SUBJECT: Status Report* 8EHQ-1284-0540 S

Approved 1/25/85

Revision Needed

FROM: David R. Williams, DRW Section 8(e) Coordinator
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Note

The submitting company has claimed its company name and the amount of each constituent in the tested mixture to be TSCA Confidential Business Information. The Information Management Division (IMD/OTS) has requested the submitter to substantiate these confidentiality claims.

Submission Description

The submitting company provided the following summarized findings from three acute rabbit dermal application studies of a mixture comprised of imidazole and 2-ethyl-4-methylimidazole:

> "A mixture of ...imidazole (CAS [No.] 288-32-4) ...[and] 2-ethyl-4-methylimidazole (CAS [No.] 931-36-2) applied at 2 Gm/Kg of body weight to the shaved skin of albino rabbits produced death in 10 of 10 animals between 4 and 24 hours after dosing. In another experiment, this effect was confirmed in the death of 3/3 animals with the same formulation but using other chemical lot numbers. In a third study, two of three animals also died using the same formulation but with ingredients supplied by another manufacturer."

In its submission, the company noted that 1) "no toxicological information exists on 2-ethyl-4-methylimidizole" and 2) "there ...[are] no dermal toxicity data on imidazole."

Submission Evaluation

In order to evaluate the significance of the reported findings, the submitter should be asked to provide a full copy of the final report (including the actual experimental protocol and data) from each of the cited acute dermal application studies. Without such information, one can only speculate about the possible cause(s) of the observed lethality: 1) the 2-ethyl-3-methylimidazole may be the more potent toxicant in the mixture; 2) there could be synergism or some type of dose-addition or response-addition between the constitutents of the mixture; 3) an unidentified toxic contaminant may be present in the mixture; and/or 4) the dermal route of exposure to the mixture could make a real difference in terms of the observed toxicity.

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

Current Production and Use

A review of the production range (includes importation volumes) statistics for imidazole (CAS No. 288-32-4), which is listed in the initial TSCA Inventory, has shown that between 101 thousand and 1 million pounds were reported as produced/imported during 1977. **/

A review of the production range (includes importation volumes) statistics for 2-ethyl-4-methylimidazole (CAS No. 931-36-2), which is listed in the initial TSCA Inventory, has shown that between 1 thousand and 13 thousand pounds were reported as produced/imported during 1977. **/

The submitting company did not provide any information concerning the current production or use(s) of the tested mixture or its components. According to secondary literature sources, imidazole is used (in many cases in combination with other chemicals) for the biological control of insects; 2-ethyl-4-methylimidazole is reportedly used in the curing of epoxy resins.

Comments/Recommendations

It should be noted that it has been EPA's longstanding position that certain types of acute animal toxicity information may not warrant submission to EPA under Section 8(e), the "substantial risk" information reporting provision of the Toxic Substances Control Act (TSCA). The basis for EPA's position is as follows:

> The preface to Part V of the Agency's March 16, 1978, TSCA Section 8(e) policy statement ("Statement of Interpretation and Enforcement Policy; Notification of Substantial Risk" 43 FR 11110) states that "a substantial risk of injury to health or the environment is a risk of considerable concern because of (a) the seriousness of the [adverse] effect ... and (b) the fact or probability of its occurrence." With regard to the seriousness of the effect, Part V explains that the Agency considers the health effects for which substantial

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**/ This production range information does not include any production/importation data claimed as TSCA Confidential Business Information (TSCA CBI) by the persons reporting for the TSCA Inventory, nor does it include any information that would compromise TSCA CBI. The data submitted for the TSCA Inventory, including production range data, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

risk information must be reported to include "any pattern of effects or evidence which reasonably supports the conclusion that the chemical substance or mixture can produce cancer, mutation, birth defects, or toxic effects resulting in death, or serious or prolonged incapacitation." Information with respect to these effects can be obtained directly or inferred from designed studies (e.g., in vivo experiments as described in Part VI of the TSCA Section 8(e) policy statement). With regard to the criterion concerning the "fact or probability" of the occurrence of such effects, Part V of the TSCA Section 8(e) policy statement explains that certain types of health effects are so serious that relatively little weight should be given to the chemical's exposure in determining whether a risk is substantial.

EPA's response to Comment 14 in Appendix B of the Section 8(e) policy statement provides guidance concerning the 8(e)-applicability of results obtained from routine acute in vivo range finding studies (e.g., LD50 determinations, skin/eye irritation tests, etc.). In its response, the Agency stated that "many routine tests are based on knowledge of toxicity associated with a chemical...." EPA's response also directed that unknown effects that occur and are observed/determined during such routine studies may have to be reported to EPA under Section 8(e) if such effects are serious and meet the reporting requirements set forth in the Section 8(e) policy statement. Thus, when evaluating the results of acute animal toxicity studies for possible submission to EPA under Section 8(e), the Agency believes that subject companies should consider such factors as the lethal dose, the pH of the tested chemical or mixture, the route of administration, the occurrence of unexpected effects (which could be determined via "cage-side" observation or during necropsy), and the extent and pattern of the actual or potential exposure to the tested chemical or mixture. In general, when evaluating such information for TSCA Section 8(e) reporting, the greater the acute toxicity, the less heavily a subject company should weigh the exposure to the tested chemical or mixture, and vice versa.

In light of the preceeding discussion, it does not appear that the acute toxicity information, as presented in this submission, warranted reporting at this stage under Section 8(e) of TSCA. In making this initial determination, however, it should be understood that the Agency may not be aware of additional pertinent information that may have been available to and/or considered by the submitting company in deciding to report the findings to EPA under Section 8(e) of TSCA.

a) The Chemical Screening Branch will request the submitting company to provide a full copy of the final report (including the actual experimental protocol and data) from each toxicity study that was cited in the submission. In addition, the submitting company will be asked to provide its rationale (in light of the discussion presented in the

Comments/Recommendations section of this report) as to why the acute *in vivo* toxicity information as presented in the submission was believed to have warranted reporting to EPA under Section 8(e) of TSCA.

In view of EPA's general interest in company actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the submitting company will be asked to describe the actions it has taken or plans to take to (1) warn workers and others, and (2) reduce or eliminate exposure to the tested chemicals. In addition, the submitting company will be requested to describe the nature of all other studies that it has conducted, is conducting, or plans to conduct that are designed to further define the toxicity of and/or the exposure to the tested mixture or its components.

b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of the subject chemicals.

c) The Chemical Screening Branch will send a copy of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OAR/EPA, ORD/EPA, and OPP/OPTS. Copies of this report will be sent also to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

8EHQ-1284-0541 S
Page 1 of 2

DATE: JAN - 9 1985

SUBJECT: Status Report* 8EHQ-1284-0541 S

Approved 1/14/85

Revision Needed ______

FROM: David R. Williams, DRW Section 8(e) Coordinator
Chemical Risk Identification Section/CSB

TO: Frank D. Kover, Branch Chief
Chemical Screening Branch/ECAD/OTS/OPTS

Note The submitting company has claimed its company name as TSCA Confidential Business Information (CBI). The Information Management Division (IMD/OTS) has requested the submitting company to substantiate this confidentiality claim.

Submission Description

The submitting company provided summarized findings from two *in vitro* genotoxicity studies of benzofurazan-1-oxide (CAS No. 480-96-6). According to the company, the chemical "tested positive for mutagenicity in both the Ames Salmonella/Microsome Plate Test (with activation) and the Mouse Lymphoma Cell Forward Mutation Assay (with and without activation)."

Submission Evaluation

It should be noted that there are several published scientific papers which present information on the genotoxic activity of benzofurazan-1-oxide in bacteria. Although the summarized information contained in this submission indicates also that the chemical possesses some degree of genotoxic activity in bacteria (as well as in cultured mouse cells), a complete copy of the final report (including the actual experimental protocol and data) from each study cited in the submission is needed in order for EPA to evaluate the significance of the reported findings.

Current Production and Use

A review of the production range (includes importation volumes) statistics for benzofurazan-1-oxide (CAS No. 480-96-6), which is listed in the initial TSCA Inventory, has shown that no 1977 production/importation was reported or that all of the production range data reported were claimed as TSCA Confidential Business Information (TSCA CBI) by the manufacturer(s) and/or importer(s) and cannot be disclosed (TSCA Section 14(a), U.S.C. 2613(a)). The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the TSCA Inventory Reporting Regulations (40 CFR 710).

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*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

The submitting company did not provide any information regarding the current production or specific use(s) of benzofurazan-1-oxide. The submitter did report, however, that the chemical is being used "on an experimental basis" by the company. According to secondary literature sources, benzofurazan-1-oxide is used as a laboratory reagent.

Comments/Recommendations

Although a positive in vitro genotoxicity test result, when considered alone, may not be sufficient to offer reasonable support for a conclusion of substantial risk, EPA believes that such results are of value in assessing the possible risks posed by chemicals to health and/or the environment. In addition, EPA believes that positive genotoxicity test results in combination with additional information (e.g., knowledge of potential exposure to or high production of the chemical substance or mixture) would suggest, in many cases, the need to conduct other studies designed to better define the toxicity of and/or exposure to the chemical substance or mixture. The results of such additional studies should be considered also for possible submission under Section 8(e) of TSCA.

(a) The Chemical Screening Branch (CSB/ECAD/OTS) will ask the submitting company to provide a full copy of the final report (including the actual experimental protocol and data) from each genotoxicity study cited in the company's submission.

In light of the Agency's general interest in corporate actions that are taken on a voluntary basis in response to chemical toxicity/exposure information, the Chemical Screening Branch will ask the submitting company to describe the actions it has taken or plans to take to 1) warn workers and others, and 2) reduce or eliminate exposure to benzofurazan-1-oxide. In addition, the submitter will be asked to describe all other studies that the company has conducted, is conducting, or plans to conduct to better define the toxicity of and/or the exposure to benzofurazan-1-oxide.

(b) The Chemical Screening Branch will review the reported information in order to determine the need for further OTS assessment of benzofurazan-1-oxide.

(c) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, FDA, CPSC, NTP, OW/EPA, OSWER/EPA, OAR/EPA, ORD/EPA, and OPP/OPTS. Copies of this report will be sent also to the TSCA Assistance Office (TAO/OTS/OPTS) for further distribution.

APPENDIX A

THURSDAY, MARCH 16, 1978
PART V

THE NATIONAL ARCHIVES OF THE UNITED STATES
1934

federal register

ENVIRONMENTAL PROTECTION AGENCY

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TOXIC SUBSTANCES CONTROL ACT

Statement of Interpretation and Enforcement Policy; Notification of Substantial Risk

[6560-01]

ENVIRONMENTAL PROTECTION AGENCY

[FRL 849-2]

TOXIC SUBSTANCES CONTROL ACT

Notification of Substantial Risk Under Section 8(e)

AGENCY: Environmental Protection Agency.

ACTION: Statement of interpretation and enforcement policy.

SUMMARY: This action states EPA's interpretation of, and enforcement policy concerning, section 8(e) of the Toxic Substances Control Act (TSCA) (90 Stat. 2029, 15 U.S.C. 2607). The provisions of that section went into effect on January 1, 1977.

Section 8(e) states that "any person who manufactures, processes, or distributes in commerce a chemical substance or mixture and who obtains information which reasonably supports the conclusion that such substance or mixture presents a substantial risk of injury to health or the environment shall immediately inform the Administrator of such information unless such person has actual knowledge that the Administrator has been adequately informed of such information."

DATES: The policy expressed in this document is in effect as of the date of publication.

FOR FURTHER INFORMATION CONTACT:

Frank D. Kover, Assessment Division, Office of Toxic Substances (WH-557), Environmental Protection Agency, 401 M Street SW., Washington, D.C. 20460, 202-755-2110.

SUPPLEMENTARY INFORMATION: On September 9, 1977, the Agency proposed guidance (42 FR 45362) on its interpretation of and policy concerning the provisions of section 8(e). Although the proposed "guidance" was an interpretive rule and statement of policy exempt from the notice and public comment provisions of the Administrative Procedure Act (5 U.S.C. 553), the Agency solicited comments on several issues to make more informed decisions. On October 11, the comment period was extended from October 15 to October 31, 1977 (42 FR 54857). On November 4, 1977, a supplemental notice to the proposed guidance was published (42 FR 57744), deleting the November 15 date for reporting certain information obtained before 1977 and stating that a new date would be established in the final guidance.

In developing this policy statement, two meetings have been held (February 1, 1977, and October 26, 1977) with selected representatives of industry and environmental and other interested groups. Comments submitted pursuant to the February 1 meeting were addressed in the preamble to the September 9 proposal. Over 100 written comments have been submitted pursuant to the September 9 proposal from trade associations, businesses, environmental groups, labor unions, State and Federal agencies, and other interested parties. Appendix B describes significant issues raised in these comments and the Agency's response to them.

The major modifications to the September 9 proposal are summarized in points 1 through 7 below.

(1) Pursuant to some question over the definition and nature of "guidance," this document is now described more accurately as a "policy statement." It is exempt from the notice and public comment provisions of the Administrative Procedure Act, as well as provisions concerning delayed effective dates.

(2) Many commenters expressed the view that to apply these requirements to officers and employees of a business organization would result in ill-considered, premature reports and would unfairly subject employees to conflicting responsibilities as individual respondents and as corporate agents. Other commenters expressed support for the view that certain employees have a responsibility to report pertinent information, and felt that the phrase "capable of appreciating pertinent information" appropriately described those employees.

The September 9 proposal would have applied section 8(e) requirements to commercial establishments as well as to employees capable of appreciating pertinent information, but stipulated enforcement priorities intended to encourage corporate processing and centralized reporting of such information (42 FR 45363). The intent was to ensure that pertinent information obtained by employees is promptly and appropriately considered, while minimizing duplicative or ill-considered submissions.

The Agency now feels that these objectives would best be served by allowing commercial establishments—under certain conditions designed to ensure full disclosure—to assume exclusive responsibility for reporting to EPA any substantial-risk information obtained by individual officers or employees. Accordingly, this policy statement stipulates that individual officers and employees will have fully discharged their section 8(e) obligations once they have notified the designated responsible company supervisor or official of pertinent information, *provided*, that the employing company or firm has established, internally publicizes, and affirmatively implements procedures governing such notifications. These procedures, at a minimum, must: (1) Specify the information that must be reported; (2) indicate how the notifications are to be prepared and submitted; (3) note the Federal penalties for failing to report; and (4) provide a mechanism for promptly notifying officers and employees who have submitted reports of the company's disposition of those reports, including whether or not they were submitted to EPA (and if not, informing employees of their right to report to EPA, as protected by TSCA section 23). EPA believes these four criteria will ensure prompt and appropriate processing of pertinent information.

Establishment of such procedures notwithstanding, all officials responsible and having authority for the organization's execution of its section 8(e) obligations retain personal liability for ensuring that substantial-risk information is reported to EPA.

(3) The September 9 proposal stated, in Part III, that a person obtains information when he is aware that it "may suggest" substantial risk. Numerous commenters questioned the Administrator's authority to compel the reporting of information which "may suggest" substantial risk. The Administrator agrees that section 8(e) addresses information that "reasonably supports the conclusion" of substantial risk and has deleted the "may suggest" provision, but emphasizes that "reasonably supports the conclusion" of substantial risk is not identical to a conclusive demonstration of substantial risk. The former typically occurs, and must be reported, at an earlier stage. Part VI in this policy statement provides Agency interpretation of the types of information that "reasonably support" such a conclusion.

(4) Numerous commenters requested clarification of different aspects of Part V of the September 9 proposal ("Information Which Reasonably Supports a Conclusion of Substantial Risk"), particularly concerning environmental effects, and suggested different interpretations of what constitutes a "substantial risk". The Agency continues to focus in this policy statement on the effects set forth in the September 9 proposal, but clarifies that the substantiality of a risk is a function of both the seriousness of the effect and the probability of its occurrence (see Part V).

(5) Numerous commenters maintained that section 8(e) only applies prospectively to information obtained after January 1, 1977. The Agency disagrees, as explained in the preamble to the September 9 proposal. This policy statement continues to apply section 8(e) to information obtained before 1977 of which a person has

been aware since January 1, 1977. In response to requests for clarification, the statement defines what constitutes such awareness. In this manner, EPA intends to limit the need for searches of historical records and files.

(6) This policy statement now provides that any information published in scientific literature, in any language, is exempt if it is referred to in abstracts published by specified abstracting services.

(7) This policy statement describes in a new Part X how to submit claims of confidentiality.

Accordingly, the Administrator's interpretation of and policy towards section 8(e) is set forth below.

Dated: February 24, 1978.

Douglas Costle,
Administrator.

I. Definitions

The definitions set forth in TSCA section 3 apply to these requirements. In addition, the following definitions are provided for purposes of this policy statement:

The term "manufacture or process 'for commercial purposes' " means to manufacture or process: (1) For distribution in commerce, including for test marketing purposes, (2) for use as a catalyst or an intermediate, (3) for the exclusive use by the manufacturer or processor, or (4) for product research and development.

The term "person" includes any natural person, corporation, firm, company, joint-venture, partnership, sole proprietorship, association, or any other business entity, any State or political subdivision thereof, any municipality, any interstate body and any department, agency, or instrumentality of the Federal Government.

The term "substantial-risk information" means information which reasonably supports the conclusion that a chemical substance or mixture presents a substantial risk of injury to health or the environment.

II. Persons Subject to the Requirement

Persons subject to section 8(e) requirements include both natural persons and business entities engaged in manufacturing, processing, or distributing in commerce a chemical substance or mixture. In the case of business entities, the president, chief executive officer, and any other officers responsible and having authority for the organization's execution of its section 8(e) obligations must ensure that the organization reports substantial-risk information to EPA. The business organization is considered to have obtained any information which any officer or employee capable of appreciating the significance of that information has obtained. It is therefore incumbent upon business organizations to establish procedures for expeditiously processing pertinent information in order to comply with the schedule set forth in Part IV.

Those officers and employees of business organizations who are capable of appreciating the significance of pertinent information are also subject to these reporting requirements. An employing organization may relieve its individual officers and employees of any responsibility for reporting substantial-risk information directly to EPA by establishing, internally publicizing, and affirmatively implementing procedures for employee submission and corporate processing of pertinent information. These procedures, at a minimum, must: (1) Specify the information that officers and employees must submit; (2) indicate how such submissions are to be prepared and the company official to whom they are to be submitted; (3) note the Federal penalties for failing to report; and (4) provide a mechanism for promptly advising officers and employees in writing of the company's disposition of the report, including whether or not the report was submitted to EPA (and if not informing employees of their right to report to EPA, as protected by TSCA section 23). An employee of any company that has established and publicized such procedures, who has internally submitted pertinent information in accordance with them, shall have discharged his section 8(e) obligation. Establishment of such procedures notwithstanding, all officials responsible and having authority for the organization's execution of its section 8(e) obligations retain personal liability for ensuring that the appropriate substantial-risk information is reported to EPA.

Business organizations that do not establish such procedures cannot relieve their individual officers and employees of the responsiblity for ensuring that substantial-risk information they obtain is reported to EPA. While officers and employees of such organizations may also elect to submit substantial-risk information to their superiors for corporate processing and reporting, rather than to EPA directly, they have not discharged their individual section 8(e) obligation until EPA has received the information.

Note.—Irrespective of a business organization's decision to establish and publicize the procedures described above, it is responsible for becoming cognizant of any substantial-risk information obtained by its officers and employees, and for ensuring that such information is reported to EPA within 15 working days.

III. When a Person Will Be Regarded as Having Obtained Information

A person obtains substantial-risk information at the time he first comes into possession of or knows of such information.

Note.—This includes information of which a prudent person similarly situated could reasonably be expected to possess or have knowledge.

An establishment obtains information at the time any officer or employee capable of appreciating the significance of such information obtains it.

IV. Requirement That a Person "Immediately Inform" the Administrator

With the exception of information on emergency incidents of environmental contamination [see Part V(c)] a person has "immediately informed" the Administrator if information is received by EPA not later than the 15th working day after the date the person obtained such information. Supplementary information generated after a section 8(e) notification should, if appropriate, be immediately reported. For emergency incidents of environmental contamination, a person shall report the incident to the Administrator by telephone as soon as he has knowledge of the incident (see Part IX for appropriate telephone contacts). The report should contain as much of the information required by Part IX as possible. A written report in accordance with Part IX (a) through (f) is to be submitted within 15 days.

Information currently in the possession of a person who is subject to reporting must be reported within 60 days of publication of this policy statement.

V. What Constitutes Substantial Risks

A "substantial risk of injury to health or the environment" is a risk of considerable concern because of (a) the seriousness of the effect [see Subparts (a), (b), and (c) below for an illustrative list of effects of concern], and (b) the fact or probability of its occurrence. (Economic or social benefits of use, or costs of restricting use, are not to be considered in determining whether a risk is "substantial".) These two criteria are differentially weighted for different types of effects. The human health effects listed in Subpart (a) below, for example, are so serious that relatively little weight is given to exposure; the mere fact the implicated chemical is in commerce constitutes sufficient evidence of exposure. In contrast, the remaining effects listed in Subparts (b) and (c) below must involve, or be accompanied by the potential for, significant levels of exposure (because of general production levels, persistence, typical uses, common means of disposal, or other pertinent factors).

Note that: (1) The effects outlined below should not be reported if the respondent has actual knowledge that the Administrator is already informed of them.

(ii) Information respecting these effects can be obtained either directly, by observation of their occurrence, or inferred from designed studies as discussed in Part VI.

The Agency considers effects for which substantial-risk information must be reported to include the following:

(a) *Human health effects*—(1) Any instance of cancer, birth defects, mutagenicity, death, or serious or prolonged incapacitation, including the loss of or inability to use a normal bodily function with a consequent relatively serious impairment of normal activities, if one (or a few) chemical(s) is strongly implicated.

(2) Any pattern of effects or evidence which reasonably supports the conclusion that the chemical substance or mixture can produce cancer, mutation, birth defects or toxic effects resulting in death, or serious or prolonged incapacitation.

(b) *Environmental effects*—(1) Widespread and previously unsuspected distribution in environmental media, as indicated in studies (excluding materials contained within appropriate disposal facilities).

(2) Pronounced bioaccumulation. Measurements and indicators of pronounced bioaccumulation heretofore unknown to the Administrator (including bioaccumulation in fish beyond 5,000 times water concentration in a 30-day exposure or having an n-octanol/water partition coefficient greater than 25,000) should be reported when coupled with potential for widespread exposure and any non-trivial adverse effect.

(3) Any non-trivial adverse effect, heretofore unknown to the Administrator, associated with a chemical known to have bioaccumulated to a pronounced degree or to be widespread in environmental media.

(4) Ecologically significant changes in species' interrelationships; that is, changes in population behavior, growth, survival, etc. that in turn affect other species' behavior, growth, or survival.

Examples include: (i) Excessive stimulation of primary producers (algae, macrophytes) in aquatic ecosystems, e.g., resulting in nutrient enrichment, or eutrophication, of aquatic ecosystems.

(ii) Interference with critical biogeochemical cycles, such as the nitrogen cycle.

(5) Facile transformation or degradation to a chemical having an unacceptable risk as defined above.

(c) *Emergency incidents of environmental contamination*—Any environmental contamination by a chemical substance or mixture to which any of the above adverse effects has been ascribed and which because of the pattern, extent, and amount of contamination (1) seriously threatens humans with cancer, birth defects, mutation, death, or serious or prolonged incapacitation, or (2) seriously threatens non-human organisms with large-scale or ecologically significant population destruction.

VI. NATURE AND SOURCES OF INFORMATION WHICH "REASONABLY SUPPORTS THE CONCLUSION" OF SUBSTANTIAL RISK

Information attributing any of the effects described in Part V above to a chemical substance or mixture is to be reported if it is one of the types listed below and if it is not exempt from the reporting requirement by reason of Part VII of this policy statement. A person is not to delay reporting until he obtains conclusive information that a substantial risk exists, but is to immediately report any evidence which "reasonably supports" that conclusion. Such evidence will generally not be conclusive as to the substantiality of the risk; it should, however, reliably ascribe the effect to the chemical.

Information from the following sources concerning the effects described in Part V will often "reasonably support" a conclusion of substantial risk. Consideration of corroborative information before reporting can only occur where it is indicated below.

(1) *Designed, controlled studies.* In assessing the quality of information, the respondent is to consider whether it contains reliable evidence ascribing the effect to the chemical. Not only should final results from such studies be reported, but also preliminary results from incomplete studies where appropriate. Designed, controlled studies include:

(i) In vivo experiments and tests.

(ii) In vitro experiments and tests. Consideration may be given to the existence of corroborative information, if necessary to reasonably support the conclusion that a chemical presents a substantial risk.

(iii) Epidemiological studies.

(iv) Environmental monitoring studies.

(2) *Reports concerning and studies of undesigned, uncontrolled circumstances.* It is anticipated here that reportable effects will generally occur in a pattern, where a significant common feature is exposure to the chemical. However, a single instance of cancer, birth defects, mutation, death, or serious incapacitation in a human would be reportable if one (or a few) chemical(s) was strongly implicated. In addition, it is possible that effects less serious than those described in Part V(a) may be preliminary manifestations of the more serious effects and, together with another triggering piece of information, constitute reportable information; an example would be a group of exposed workers experiencing dizziness together with preliminary experimental results demonstrating neurological dysfunctions.

Reports and studies of undesigned circumstances include:

(i) Medical and health surveys.

(ii) Clinical studies.

(iii) Reports concerning and evidence of effects in consumers, workers, or the environment.

VII. INFORMATION WHICH NEED NOT BE REPORTED

Information need not be reported if it:

(a) Has been published by EPA in reports;

(b) Has been submitted in writing to EPA pursuant to mandatory reporting requirements under TSCA or any other authority administered by EPA (including the Federal Insecticide, Fungicide and Rodenticide Act, the Clean Air Act, the Federal Water Pollution Control Act, the Marine Protection, Research, and Sanctuaries Act, the Safe Drinking Water Act, and the Resource Conservation and Recovery Act), provided that the information: (1) Encompasses that required by Part IX (c) through (f); and (2) is from now on submitted within the time constraints set forth in Part IV and identified as a section 8(e) notice in accordance with Part IX(b);

(c) Has been published in the scientific literature and referenced by the following abstract services: (1) Agricola, (2) Biological Abstracts, (3) Chemical Abstracts, (4) Dissertation Abstracts, (5) Index Medicus, (6) National Technical Information Service.

(d) Is corroborative of well-established adverse effects already documented in the scientific literature and referenced as described in (c) above, unless such information concerns emergency incidents of environmental contamination as described in Part V(c), or

(e) Is contained in notification of spills under section 311(b)(5) of the Federal Water Pollution Control Act.

VIII. INFORMATION FIRST RECEIVED BY A PERSON PRIOR TO THE EFFECTIVE DATE OF TSCA

Any substantial risk information possessed by a person prior to January 1, 1977, of which he is aware after that date shall be reported within 60 days of publication of this policy statement. The Agency considers that a person is "aware" of:

(a) Any information reviewed after January 1, 1977, including not only written reports, memoranda and other documents examined after January 1, 1977, but also information referred to in discussions and conferences in which the person participated after January 1, 1977;

(b) Any information the contents of which a person has been alerted to by date received after January 1, 1977, including any information concerning a chemical for which the person is presently assessing health and environmental effects;

(c) Any other information of which the person has actual knowledge.

IX. Reporting Requirements

Notices shall be delivered to the Document Control Officer, Chemical Information Division, Office of Toxic Substances (WH-557), Environmental Protection Agency, 401 M Street SW., Washington, D.C. 20460.

A notice should:

(a) Be sent by certified mail, or in any other way permitting verification of its receipt by the Agency,

(b) State that it is being submitted in accordance with section 8(e),

(c) Contain the job title, name, address, telephone number, and signature of the person reporting and the name and address of the manufacturing, processing, or distributing establishment with which he is associated,

(d) Identify the chemical substance or mixture (including, if known, the CAS Registry Number),

(e) Summarize the adverse effects being reported, describing the nature and the extent of the risk involved, and

(f) Contain the specific source of the information together with a summary and the source of any available supporting technical data.

For emergency incidents of environmental contamination (see Part V(c)), a person shall report the incident to the Administrator by telephone as soon as he has knowledge of the incident (see below for appropriate telephone contacts). The report should contain as much of the information required by instructions (b) through (f) above as possible. A written report, in accordance with instructions (a) through (f) above, is to be submitted within 15 days. Twenty-four hour emergency telephone numbers are:

Region I (Maine, Rhode Island, Connecticut, Vermont, Massachusetts, New Hampshire), 617-223-7265.
Region II (New York, New Jersey, Puerto Rico, Virgin Islands), 201-548-8730.
Region III (Pennsylvania, West Virginia, Virginia, Maryland, Delaware, District of Columbia), 215-597-9898.
Region IV (Kentucky, Tennessee, North Carolina, South Carolina, Georgia, Alabama, Mississippi, Florida), 404-881-4062.
Region V (Wisconsin, Illinois, Indiana, Michigan, Ohio, Minnesota), 312-353-2318.
Region VI (New Mexico, Texas, Oklahoma, Arkansas, Louisiana), 214-749-3840.
Region VII (Nebraska, Iowa, Missouri, Kansas), 816-374-3778.
Region VIII (Colorado, Utah, Wyoming, Montana, North Dakota, South Dakota), 303-837-3880.
Region IX (California, Nevada, Arizona, Hawaii, Guam), 415-556-6254.
Region X (Washington, Oregon, Idaho, Alaska), 206-442-1200.

X. Confidentiality Claims

(a) Any person submitting a notice to EPA under section 8(e) of TSCA may assert a business confidentiality claim covering all or part of the information contained in the notice. Any information covered by a claim will be disclosed by EPA only to the extent, and by means of the procedures, set forth in 40 CFR Part 2 (41 FR 36902, September 1, 1976).

(b) If no claim accompanies the notice at the time it is submitted to EPA, the notice will be placed in an open file to be available to the public without further notice to the submitter.

(c) To assert a claim of confidentiality for information contained in a notice, the submitter must submit two copies of the notice.

(1) One copy must be complete. In that copy the submitter must indicate what information, if any, is claimed as confidential by marking the specified information on each page with a label such as "confidential," "proprietary," or "trade secret."

(2) If some information in the notice is claimed as confidential, the submitter must submit a second copy. The second copy must be complete except that all information claimed as confidential in the first copy must be deleted.

(3) The first copy of the notice will be disclosed by EPA only to the extent, and by means of the procedures, set forth in 40 CFR Part 2. The second copy will be placed in an open file to be available to the public.

(d) Any person submitting a notice containing information for which they are asserting a confidentiality claim should send the notice in a double envelope.

(1) The outside envelope should bear the same address outlined in section IX of this policy statement.

(2) The inside envelope should be clearly marked "To be opened only by the OTS Document Control Officer."

XI. Failure To Report Information

Section 15(3) of TSCA makes it unlawful for any person to fail or refuse to submit information required under section 8(e). Section 16 provides that a violation of section 15 renders a person liable to the United States for a civil penalty and possible criminal prosecution. Pursuant to section 17, the Government may seek judicial relief to compel submittal of section 8(e) information and to otherwise restrain any violation of section 8(e).

Appendix A.—Quick Reference Summary for Emergency Incidents of Environmental Contamination

A. WHAT SHOULD BE REPORTED AS AN EMERGENCY INCIDENT

An emergency incident of environmental contamination is "any environmental contamination by a chemical substance or mixture . . . which, because of the pattern, extent and amount of contamination, (1) Seriously threatens humans with cancer, birth defects, mutation, death, or serious or prolonged incapacitation, or (2) seriously threatens non-human organisms with large scale or ecologically significant population destruction". (See Part V(c) for complete description.)

B. WHAT NEED NOT BE REPORTED AS AN EMERGENCY INCIDENT

Information contained in notification of spills under section 311(b)(5) of the Federal Water Pollution Control Act (FWPCA). (For a complete list of exemptions to reporting, see Part VII.)

C. WHEN AND WHERE TO REPORT EMERGENCY INCIDENTS

Emergency incidents of environmental contamination are to be reported immediately by telephone to the appropriate EPA Regional 24-hour telephone emergency line listed below.

Region I (Maine, Rhode Island, Connecticut, Vermont, Massachusetts, New Hampshire), 617-223-7265.
Region II (New York, New Jersey, Puerto Rico, Virgin Islands), 201-548-8730.
Region III (Pennsylvania, West Virginia, Virginia, Maryland, Delaware, District of Columbia), 215-597-9898.
Region IV (Kentucky, Tennessee, North Carolina, South Carolina, Georgia, Alabama, Mississippi, Florida), 404-881-4062.
Region V (Wisconsin, Illinois, Indiana, Michigan, Ohio, Minnesota), 312-353-2318.
Region VI (New Mexico, Texas, Oklahoma, Arkansas, Louisiana), 214-749-3840.
Region VII (Nebraska, Iowa, Missouri, Kansas), 816-374-3778.
Region VIII (Colorado, Utah, Wyoming, Montana, North Dakota, South Dakota), 303-837-3880.
Region IX (California, Nevada, Arizona, Hawaii, Guam), 415-556-6254.
Region X (Washington, Oregon, Idaho, Alaska), 206-442-1200.

In addition, a written report, in accordance with instructions (a) through (f) of Part IX, is to be submitted within 15 days to the Document Control Officer, Chemical Information Division, Office of Toxic Substances (WH-557), 401 M Street SW., Washington, D.C. 20460.

Appendix B—Significant Comments and Responses

A. PERSONS SUBJECT TO THESE REQUIREMENTS

Comment 1: Employees cannot be held subject to these requirements, since: (a) They only have a partial role in the manufacture, processing, or distribution of chemicals, (b) in other sections of TSCA, the term "person who manufactures, processes, or distributes" chemicals clearly refers to business organizations; "persons" should be consistently defined, and (c) the application of criminal penalties mandates a strict interpretation of this word.

Response: The Agency considers that different sections of TSCA, having different purposes, are appropriately directed to different respondents. In the case of section 8(e), officers and employees who are capable of appreciating the significance of information have a legitimate responsibility to be alert to and report substantial-risk information. The guidance has been modified so that natural persons and business entities can fulfill their section 8(e) obligations in different ways. Most officers and employees can discharge their section 8(e) obligations by submitting pertinent information to corporate superiors, provided that the company has established the risk-evaluation procedures characterized in Part II. In the case of a business organization, its president, chief executive officer, and other officials responsible and having authority for the business organization's execution of its section 8(e) obligations must ensure that the organization reports substantial-risk information to EPA.

Comment 2: Even if employees can be held subject to these requirements, they should not be. To do so would force employees and employers into conflicting positions, inviting internal corporate dissension and over- reporting. Further, individuals often do not have the overview necessary to reach considered, well-supported decisions. Corporate reporting by designated officials will provide EPA with more reliable data.

Response: The Agency considers that employees have a legitimate role in risk reporting; it is imperative that risk information obtained by employees be appropriately considered. Officers and employees can fulfill their role in the reporting of substantial-risk information, without the disadvantages described above, by reporting information to superiors for corporate consideration, and, having done so, will have discharged their obligation to EPA. This is contingent upon the establishment by the business organization of certain procedures for risk-evaluation, thereby assuring the appropriate consideration of such reports. Those officers responsible and having authority for the organization's execution of its section 8(e) obligations must ensure that the organization reports substantial-risk information to EPA.

Comment 3: Clarify which employees are covered, and the extent of their obligation. Are employees "capable of appreciating pertinent information" by virtue of rank, or knowledge? Are rank and file employees subject to these requirements, or just supervisory and managerial personnel, company toxicologists, etc.? Is an employee absolved of further responsibility if he reports to his supervisor?

Response: The Agency considers that the phrase "capable of appreciating the significance of pertinent information" appropriately describes those officers and employees who have a responsibility to be alert to and report substantial-risk information, including not only relatively senior corporate officers but also many corporate employees. The policy statement modifies the September 9 proposal, in response to the concerns expressed in Comments 2 and 3, to permit most officers and employees to discharge their obligation by submitting information to corporate superiors, subject to the conditions described in Part II.

Comment 4: Consultants and independent labs should not be subject to these requirements.

Response: Contractors and independent labs are not responsible for reporting information they have obtained directly to EPA; rather, their client manufacturers, processors and distributors are responsible for reporting such information.

B. THE "OBTAINING" OF INFORMATION

Comment 5: The "may suggest" criterion in Part III of the proposal serves to compel further examination of information that by itself is not subject to section 8(e) requirements. The statutory language calling for "reasonable support" does not support this. Further, risk assessment often requires anywhere from months to several years of study after preliminary results "suggest" risk, far exceeding the 15-day compliance period.

Response: The Agency does not intend to compel under section 8(e) examination of information that by itself is not subject to section 8(e) requirements and has deleted the "may suggest" provision, providing its interpretation of what constitutes evidence that "reasonably supports the conclusion" of substantial risk in a new Part VI.

Comment 6: Section 8(e) obligations are incurred upon obtaining conclusory substantial-risk information.

Response: The Agency disagrees, and considers that "reasonable support" of a conclusion of substantial risk is not identical to the conclusion itself. The former typically occurs, and must be reported, at an earlier stage.

Comment 7: The statement, in Part III of the proposal that a person has obtained information if he ". . . should know of the existence of such information not in his possession but which would be delivered to him on request," tends to compel an active search for substantial-risk information rather than the reporting of substantial-risk information a person "obtains." This is of particular concern to importers with limited access to information possessed by their suppliers.

Response: The Agency considers that section 8(e) applies to information which a person possesses or of which he knows. It is not intended to compel searches for information or extraordinary efforts to acquire information. The Agency further considers, however, that "known" information includes information which a prudent person similarly situated could reasonably be expected to know. Negligence or intentional avoidance of information does not absolve a person of his section 8(e) obligation. Part III has been modified to express these intentions.

Comment 8: Circumstances can exist when coming "into possession" of risk information does not correspond to an understanding of the implications of the information; "obtains" should be defined in terms of possession of information and awareness of its import.

Response: The "obtaining" of information occurs via persons who are "capable of appreciating the significance of pertinent information." There will likely be circumstances in which the evaluation of information clarifies its full import; the establishment of corporate procedures for processing risk-information prescribed in Part II will expedite this.

C. TIME ALLOWED FOR COMPLIANCE

Comment 9: Fifteen calendar days is insufficient to determine whether information which "may suggest" substantial risk should be reported; it is even insufficient to accommodate normal procedural time constraints (corporate processing, mailing, holidays, etc.).

Response: The Agency has changed the compliance period to 15 business days. It is imperative that procedures be established to expedite the reporting of substantial-risk information, not that reporting conform to existing procedures.

Comment 10: Allow from 30 to 90 days for the second phase of reporting; alternatively, do not prescribe a time limit for additional reporting.

Response: Having deleted the "may suggest" criterion, the Agency sees no need to provide a second phase to the reporting period. Supplemental information that is generated after a section 8(e) notification should, if appropriate, be immediately reported.

Comment 11: Allow from 30 to 120 days to report pre-1977 information; this period should commence: (a) upon final publication, (b) January 1, 1978, (c) following the inventory reporting period since many of the same corporate personnel will be implementing both requirements.

Response: The policy statement prescribes a 60 day reporting period, commencing immediately upon publication. Section 8(e) has been in effect since January 1, 1977; postponement in reporting substantial-risk information is not warranted.

D. EFFECTS AND INFORMATION THAT MUST BE REPORTED

Comment 12: The reporting of "any instance" of cancer, birth defects, etc., in humans is too broad and such information will be of little use; chemical workers, like the general population, develop cancers and other ailments of uncertain etiology.

Response: This policy statement clarifies that the reporting of single occurrences of human cancer or other serious effects will depend upon evidence strongly implicating one (or a few) chemical(s).

Comment 13: Dermal ailments and nausea are poorly chosen examples of precursor symptoms. Deleting these examples will avoid unduly emphasizing them when other symptoms may be more important, yet will not eliminate the obligation to report them if they are suspected precursors.

Response: The Agency agrees.

Comment 14: How are reportable data distinguished from routine tests including range tests such as LD_{50}'s?

Response: This policy statement directs the reporting of specified effects when unknown to the Administrator. Many routine tests are based on a knowledge of toxicity associated with a chemical; unknown effects occurring during such a range test may have to be reported if they are those of concern to the Agency and if the information meets the criteria set forth in Parts V and VI.

Comment 15: The most widespread "in vitro" test is the Ames test, which is subject to considerable debate. Clarify the circumstances under which positive results of in vitro tests must be reported.

Response: Part VI clarifies that the reporting of in vitro tests will depend upon the existence of corroborative information if necessary to reasonably support the conclusion of substantial risk.

Comment 16: The description of "extreme persistence" as a substantial risk is an example of the need to redefine Part V(c) ("Environmental Effects"). Persistence and bioaccumulation should be considered risks only when coupled with toxicity and significant exposure.

Response: Part V now clarifies those effects for which reporting depends upon a significant exposure potential. Persistence by itself is no longer itemized as a reportable effect but rather is considered to be a component of exposure potential; it may also underlie the measurements described in Part V(b)(1). Laboratory indicators of pronounced bioaccumulation are to be reported when coupled with potential for widespread exposure and any non-trivial adverse effect.

Comment 17: The n-octanol/water partition coefficient addresses a physico-chemical property, not biological effects, and is not alone an indicator of substantial risk; further, the values stated for the coefficient and the bioaccumulation factor in fish do not correspond.

Response: The Agency acknowledges the numerical error and has amended the values to correspond. This policy statement now directs the reporting of an experimental measurement of bioaccumulation when coupled with an adverse effect and potential for widespread exposure.

Comment 18: The requirement that information which "links" an effect to a chemical be reported is too broad and contradicts the statutory language of "reasonably supports".

Response: The Agency has provided in a new Part VI its interpretation of "reasonably supports".

Comment 19: A determination that information "reasonably supports the conclusion" of substantial risk cannot be made independently of considerations of use since the method and manner of using a chemical may influence the occurrence of an effect; in particular, the criteria should reflect a distinction between normal and abnormal uses of chemicals.

Response: The Agency considers that the appropriate components of a "substantial risk" with respect to a chemical are (a) the seriousness of the effect, and (b) total exposure potential. The method and manner of using a chemical is one of several factors determining its exposure potential. As described in Part V, the importance of exposure potential as a component of "substantial risk" depends upon the kind of effect of concern. Thus, the effects described in Part V(a) are so serious that relatively little weight is given to exposure; the effects described in Parts V (b) and (c) involve a significant exposure or exposure potential.

The Agency further considers that a definition of "normal" use for a particular chemical will often depend upon a knowledge of the risks associated with the chemical.

E. INFORMATION THAT NEED NOT BE REPORTED

Comment 20: Information published in scientific literature in languages other than English should be exempted if published in summary form by abstracting services. Can the accuracy of English language abstracts and commercial translations of foreign literature be assumed?

Response: This policy statement now provides that information published in scientific literature, whether in English or another language, is exempt from reporting if published in summary form by certain specified abstract services.

Comment 21: Information exchange systems with other Federal agencies should be immediately established so that respondents need not report to EPA information already reported to other Agencies, and vice versa. Such duplicative reports are unduly burdensome.

Response: EPA is coordinating this program with other agencies now. When this coordination is successfully completed, the policy statement will be amended to exempt from the reporting requirement information that has been submitted to other specified agencies. In the meantime, substantial-risk information must be reported directly to EPA; such a report does not discharge any reporting obligation to other agencies.

F. INFORMATION FIRST RECEIVED PRIOR TO THE EFFECTIVE DATE OF TSCA

Comment 22: The tense of the verb "obtains" reveals that section 8(e) was intended to be applied prospectively to information newly acquired after January 1, 1977. Utilize section 8(d) or other rules to acquire information obtained before then.

Response: As discussed in the preamble to the September 9 proposal, the Agency considers section 8(e) to apply to risk information possessed by or known to a person before, on, or after January 1, 1977. Concerning information first obtained before 1977, this policy statement continues to require reporting of information received if a person has been aware of it since January 1, 1977, for the reasons discussed in the September 9 preamble.

Comment 23: The term "aware" is too vague to be of any help in responding to these requirements. Since many corporate employees are potentially subject to these requirements, and given uncertainty over the extent to which they ought to be aware of pre-1977 information, this provision tends to compel the very file search it was intended to avoid. The term "aware" should be further defined, possibly in terms of actual knowledge.

Response: The Agency in Part VIII of this policy statement now defines the pre-1977 information of which a person is considered to be aware.

G. CONFIDENTIAL INFORMATION

Comment 24: EPA should delay guidance until procedures are published governing the treatment of confidential submissions.

Comment 25: EPA should treat all submissions as confidential until the information is verified.

Comment 26: EPA should automatically publish section 8(e) notices.

Response to Comments 24 through 26: EPA has included a new Part X which describes how to submit a claim of confidentiality and states that any or all of the information submitted may be claimed as confidential. Such information will be disclosed by EPA only to the extent, and by means of the procedures, set forth in 40 CFR Part 2.

H. MISCELLANEOUS

Comment 27: What is the statutory basis or need for guidance? What is its exact status under the Administrative Procedure Act?

Response: This policy statement sets forth EPA's interpretation of and policy concerning TSCA section 8(e). As an interpretive rule and statement of policy it is not subject to the comment period and delayed effective date provisions of the Administrative Procedure Act (5 U.S.C. 553). Although TSCA does not mandate a policy statement, the Agency of necessity must develop the criteria which will govern enforcement activities. Trade associations and businesses were among those who previously expressed interest in such a statement to guide their compliance.

Comment 28: Clarify whether these requirements apply to chemicals previously but no longer manufactured, processed, or distributed in commerce by a person.

Response: Information obtained before 1977 must be reported if the person has been aware of it since January 1, 1977, as prescribed by Part VIII. Concerning chemicals which a person has discontinued manufacturing, processing, or distributing since January 1, 1977, information obtained before the time of discontinuation is subject to these requirements. It is expected that the acquisition of information after that time will be minimal; however, should additional information be acquired, it may trigger the reporting described in Part VIII.

Comment 29: Clarify the meaning of "substantial risk" relative to other risks addressed by TSCA.

Response: A substantial risk is defined in Part V(a) of this policy statement as a risk of considerable concern because of (a) the seriousness of the effect, and (b) the fact or probability of its occurrence. As opposed to other risks addressed by TSCA, economic or social benefits of use, or costs of restricting use, are not to be considered in determining whether a risk is "substantial".

Comment 30: To what extent are "users" of chemicals subject to these requirements?

Response: The Agency considers that many industrial uses of chemicals actually fall within the scope of "processing" chemicals. A manufacturer, processor, or distributor who obtains substantial-risk information concerning chemicals he handles should be alert to the possibility he may have to report it.

Comment 31: Are chemicals manufactured, processed and distributed in commerce in small quantities solely for purposes of research and development subject to these requirements?

Response: In general, the Agency considers that much manufacturing, processing, and distribution in commerce of chemicals in small quantities solely for purposes of research and development is conducted for "commercial purposes". Such purposes would include the sale and distribution of such materials, as well as their use by the manufacturer or processor in activities (for example, product research and development and studies assessing the feasibility and safety of using chemicals) preceding his or a client's commercial use of such materials or others on a larger scale.

As described in Part V, the Agency considers that "substantial risks" depend in part upon an exposure potential. Thus, the occurrence of the effects described in Part V(a) presuppose exposure to the chemical and must be reported; reporting of the other effects will depend upon a potential for significant levels of exposure.

Comment 32: Are raw materials, intermediates, and inert ingredients produced or used in the manufacture of a pesticide subject to TSCA?

Response: The Administrator considers that raw materials, intermediates and inert ingredients produced or used in the manufacture of a pesticide are substances or mixtures which can be regulated under TSCA.

In order to be considered a pesticide, a substance must be intended for use as a pesticide. Raw materials, intermediates, and inert ingredients produced or used in the manufacture of a pesticide are not themselves regulated under FIFRA (unless they happen to be pesticides themselves) and, therefore, are subject to TSCA. The pesticide regulations at 40 CFR 162.4 are consistent with this view.

Comment 33: Are intermediates and catalysts intended solely for use in the production of a food, food additive, drug, cosmetic, or device subject to TSCA?

Response: The Administrator considers that intermediates and catalysts intended solely for use in the production of a food, food additive, drug, cosmetic, or device are excluded from regulation under TSCA. The definitions of the FFDCA provide that chemical substances which are intended for use as a component of a food, food additive, drug, cosmetic, or device are encompassed within the meaning of such terms, respectively. The FDA considers intermediates and catalysts to be such components. Therefore, they are subject to regulation under the FFDCA. Any such substance is excluded from regulation under TSCA insofar as it is actually manufactured, processed, or distributed in commerce solely for use in the production of a food, food additive, drug, cosmetic, or device.

Comment 34: Employees should have the option to submit reports anonymously.

Response: EPA considers that any person may report information to EPA under TSCA. Those who are required to do so under section 8(e) are persons who manufacture, process, or distribute in commerce chemical substances or mixtures, including not only business entities but also such employees as described in Part II. In order to establish that such persons have discharged their obligations, and in order to encourage responsible review of the quality of information and the substantiality of risks, EPA believes that notifiers should identify themselves. Section 23 will adequately protect employees from discrimination pursuant to notifications they have made under section 8(e).

[FR Doc. 78-7064 Filed 3-15-78; 8:45 am]

APPENDIX B: STATUS REPORTS BY CAS NUMBER

CAS NUMBER: 50-00-0 CHEMICAL NAME: FORMALDEHYDE
SUBMISSION #: 8EHQ-0383-0474

CAS NUMBER: 51-78-5 CHEMICAL NAME: PHENOL, 4-AMINO-, HYDROCHLORIDE
SUBMISSION #: 8EHQ-0484-0513

CAS NUMBER: 62-53-3 CHEMICAL NAME: BENZENAMINE
SUBMISSION #: 8EHQ-0484-0513

CAS NUMBER: 64-67-5 CHEMICAL NAME: SULFURIC ACID, DIETHYL ESTER
SUBMISSION #: 8EHQ-1083-0509

CAS NUMBER: 67-56-1 CHEMICAL NAME: METHANOL
SUBMISSION #: 8EHQ-0484-0513

CAS NUMBER: 71-55-6 CHEMICAL NAME: ETHANE, 1,1,1-TRICHLORO-
SUBMISSION #: 8EHQ-1084-0535

CAS NUMBER: 74-87-3 CHEMICAL NAME: METHANE, CHLORO-
SUBMISSION #: 8EHQ-1083-0499

CAS NUMBER: 75-07-0 CHEMICAL NAME: ACETALDEHYDE
SUBMISSION #: 8EHQ-0383-0474

APPENDIX B: STATUS REPORTS BY CAS NUMBER (CONT.)

CAS NUMBER: 75-09-2 CHEMICAL NAME: METHANE, DICHLORO-
SUBMISSION #: 8EHQ-0884-0525

CAS NUMBER: 75-09-2 CHEMICAL NAME: METHYLENE CHLORIDE
SUBMISSION #: 8EHQ-0884-0525

CAS NUMBER: 75-28-5 CHEMICAL NAME: PROPANE, 2-METHYL-
SUBMISSION #: 8EHQ-0484-0511

CAS NUMBER: 76-13-1 CHEMICAL NAME: ETHANE, 1,1,2-TRICHLORO-1,2,2-TRIFLUORO-
SUBMISSION #: 8EHQ-1084-0535

CAS NUMBER: 76-13-1 CHEMICAL NAME: FREON 113
SUBMISSION #: 8EHQ-1084-0535

CAS NUMBER: 79-06-1 CHEMICAL NAME: ACRYLAMIDE
SUBMISSION #: 8EHQ-0783-0488

CAS NUMBER: 79-06-1 CHEMICAL NAME: 2-PROPENAMIDE
SUBMISSION #: 8EHQ-0783-0488

CAS NUMBER: 87-66-1 CHEMICAL NAME: 1,2,3-BENZENETRIOL
SUBMISSION #: 8EHQ-1284-0539

CAS NUMBER: 87-66-1 CHEMICAL NAME: PYROGALLOL
SUBMISSION #: 8EHQ-1284-0539

APPENDIX B: STATUS REPORTS BY CAS NUMBER (CONT.)

CAS NUMBER: 89-62-3 CHEMICAL NAME: BENZENAMINE, 4-METHYL-2-NITRO-
SUBMISSION #: 8EHQ-1083-0496

CAS NUMBER: 92-43-3 CHEMICAL NAME: PHENIDONE
SUBMISSION #: 8EHQ-0984-0529

CAS NUMBER: 92-43-3 CHEMICAL NAME: 3-PYRAZOLIDINONE, 1-PHENYL-
SUBMISSION #: 8EHQ-0984-0529

CAS NUMBER: 98-07-7 CHEMICAL NAME: BENZENE, (TRICHLOROMETHYL)-
SUBMISSION #: 8EHQ-0884-0523

CAS NUMBER: 98-82-8 CHEMICAL NAME: BENZENE, (1-METHYLETHYL)-
SUBMISSION #: 8EHQ-1184-0536

CAS NUMBER: 98-82-8 CHEMICAL NAME: CUMENE
SUBMISSION #: 8EHQ-1184-0536

CAS NUMBER: 98-88-4 CHEMICAL NAME: BENZOYL CHLORIDE
SUBMISSION #: 8EHQ-0884-0523

CAS NUMBER: 98-95-3 CHEMICAL NAME: BENZENE, NITRO-
SUBMISSION #: 8EHQ-0484-0513

CAS NUMBER: 100-44-7 CHEMICAL NAME: BENZENE, (CHLOROMETHYL)-
SUBMISSION #: 8EHQ-0884-0523

APPENDIX B: STATUS REPORTS BY CAS NUMBER (CONT.)

CAS NUMBER: 100-65-2 CHEMICAL NAME: BENZENAMINE, N-HYDROXY-
SUBMISSION #: 8EHQ-0484-0513

CAS NUMBER: 103-33-3 CHEMICAL NAME: DIAZENE, DIPHENYL-
SUBMISSION #: 8EHQ-0484-0513

CAS NUMBER: 106-89-8 CHEMICAL NAME: EPICHLOROHYDRIN
SUBMISSION #: 8EHQ-0584-0518 S

CAS NUMBER: 106-89-8 CHEMICAL NAME: OXIRANE, (CHLOROMETHYL)-
SUBMISSION #: 8EHQ-0584-0518 S

CAS NUMBER: 106-97-8 CHEMICAL NAME: BUTANE
SUBMISSION #: 8EHQ-0484-0511

CAS NUMBER: 106-98-9 CHEMICAL NAME: 1-BUTENE
SUBMISSION #: 8EHQ-0484-0511

CAS NUMBER: 106-99-0 CHEMICAL NAME: 1,3-BUTADIENE
SUBMISSION #: 8EHQ-0484-0511

CAS NUMBER: 108-10-1 CHEMICAL NAME: 2-PENTANONE, 4-METHYL-
SUBMISSION #: 8EHQ-1084-0535

CAS NUMBER: 109-52-4 CHEMICAL NAME: PENTANOIC ACID
SUBMISSION #: 8EHQ-0584-0514

APPENDIX B: STATUS REPORTS BY CAS NUMBER (CONT.)

CAS NUMBER: 111-07-9 CHEMICAL NAME: HEXADECANOIC ACID, 2-METHOXYETHYL ESTER
SUBMISSION #: 8EHQ-1084-0534

CAS NUMBER: 111-14-8 CHEMICAL NAME: HEPTANOIC ACID
SUBMISSION #: 8EHQ-0584-0514

CAS NUMBER: 111-76-2 CHEMICAL NAME: ETHANOL, 2-BUTOXY-
SUBMISSION #: 8EHQ-0483-0475 8EHQ-0584-0517

CAS NUMBER: 112-05-0 CHEMICAL NAME: NONANOIC ACID
SUBMISSION #: 8EHQ-0584-0514

CAS NUMBER: 115-11-7 CHEMICAL NAME: 1-PROPENE, 2-METHYL-
SUBMISSION #: 8EHQ-0484-0511

CAS NUMBER: 122-99-6 CHEMICAL NAME: ETHANOL, 2-PHENOXY-
SUBMISSION #: 8EHQ-0884-0528

CAS NUMBER: 123-30-8 CHEMICAL NAME: PHENOL, 4-AMINO-
SUBMISSION #: 8EHQ-0484-0513

CAS NUMBER: 288-32-4 CHEMICAL NAME: 1H-IMIDAZOLE
SUBMISSION #: 8EHQ-1284-0540 S *

CAS NUMBER: 382-10-5 CHEMICAL NAME: 1-PROPENE, 3,3,3-TRIFLUORO-2-(TRIFLUOROMETHYL)-
SUBMISSION #: 8EHQ-0483-0476 S

APPENDIX B: STATUS REPORTS BY CAS NUMBER (CONT.)

CAS NUMBER: 480-96-6 CHEMICAL NAME: BENZOFURAZAN, 1-OXIDE
SUBMISSION #: 8EHQ-1284-0541 S

CAS NUMBER: 495-48-7 CHEMICAL NAME: DIAZENE, DIPHENYL-, 1-OXIDE
SUBMISSION #: 8EHQ-0484-0513

CAS NUMBER: 540-63-6 CHEMICAL NAME: 1,2-ETHANEDITHIOL
SUBMISSION #: 8EHQ-0683-0481

CAS NUMBER: 931-36-2 CHEMICAL NAME: 1H-IMIDAZOLE, 2-ETHYL-4-METHYL-
SUBMISSION #: 8EHQ-1284-0540 S *

CAS NUMBER: 959-52-4 CHEMICAL NAME: 1,3,5-TRIAZINE, HEXAHYDRO-1,3,5-TRIS(1-OXO-2-PROPENYL)-
SUBMISSION #: 8EHQ-0384-0506 S

CAS NUMBER: 1116-54-7 CHEMICAL NAME: ETHANOL, 2,2'-(NITROSOIMINO)BIS-
SUBMISSION #: 8EHQ-0283-0469 S

CAS NUMBER: 1116-54-7 CHEMICAL NAME: N-NITROSODIETHANOLAMINE
SUBMISSION #: 8EHQ-0283-0469 S

CAS NUMBER: 1134-36-7 CHEMICAL NAME: [1,1'-BIPHENYL]-4-OL, 3-AMINO-
SUBMISSION #: 8EHQ-1083-0495

CAS NUMBER: 1143-72-2 CHEMICAL NAME: METHANONE, PHENYL(2,3,4-TRIHYDROXYPHENYL)-
SUBMISSION #: 8EHQ-0484-0510

APPENDIX B: STATUS REPORTS BY CAS NUMBER (CONT.)

CAS NUMBER: 1318-00-9 CHEMICAL NAME: VERMICULITE
SUBMISSION #: 8EHQ-0383-0473

CAS NUMBER: 1336-36-3 CHEMICAL NAME: 1,1'-BIPHENYL, CHLORO DERIVS.
SUBMISSION #: 8EHQ-0784-0521 S

CAS NUMBER: 1336-36-3 CHEMICAL NAME: POLYCHLORINATED BIPHENYLS (PCB)
SUBMISSION #: 8EHQ-0784-0521 S

CAS NUMBER: 1429-50-1 CHEMICAL NAME: PHOSPHONIC ACID, [1,2-ETHANEDIYLBIS[NITRILOBIS(METHYLENE)]]TETRAKIS-
SUBMISSION #: 8EHQ-0683-0483 S

CAS NUMBER: 2386-87-0 CHEMICAL NAME: 7-OXABICYCLO[4.1.0]HEPTANE-3-CARBOXYLIC ACID, 7-OXABICYCLO[4.1.0]HEPT-3-YLMETHYL ESTER
SUBMISSION #: 8EHQ-0784-0522

CAS NUMBER: 2426-08-6 CHEMICAL NAME: BUTYL GLYCIDYL ETHER
SUBMISSION #: 8EHQ-0584-0518 S

CAS NUMBER: 2426-08-6 CHEMICAL NAME: OXIRANE, (BUTOXYMETHYL)-
SUBMISSION #: 8EHQ-0584-0518 S

CAS NUMBER: 24[illegible]62-9 CHEMICAL NAME: ARALDITE PT-810
SUBMISSION #: 8EHQ-0[illegible]3-0490

APPENDIX B: STATUS REPORTS BY CAS NUMBER (CONT.)

CAS NUMBER: 2451-62-9 CHEMICAL NAME: 1,3,5-TRIAZINE-2,4,6(1H,3H,5H)-TRIONE, 1,3,5-TRIS(OXIRANYLMETHYL)-

SUBMISSION #: 8EHQ-0883-0490

CAS NUMBER: 2530-85-0 CHEMICAL NAME: 2-PROPENOIC ACID, 2-METHYL-, 3-(TRIMETHOXYSILYL)PROPYL ESTER

SUBMISSION #: 8EHQ-0884-0524

CAS NUMBER: 2530-85-0 CHEMICAL NAME: SILANE A-174

SUBMISSION #: 8EHQ-0884-0524

CAS NUMBER: 3033-77-0 CHEMICAL NAME: G-MAC

SUBMISSION #: 8EHQ-1283-0503

CAS NUMBER: 3033-77-0 CHEMICAL NAME: OXIRANEMETHANAMINIUM, N,N,N-TRIMETHYL-, CHLORIDE

SUBMISSION #: 8EHQ-1283-0503

CAS NUMBER: 3327-22-8 CHEMICAL NAME: 1-PROPANAMINIUM, 3-CHLORO-2-HYDROXY-N,N,N-TRIMETHYL-, CHLORIDE

SUBMISSION #: 8EHQ-1283-0503

CAS NUMBER: 5915-41-3 CHEMICAL NAME: TERBUTHYLAZINE

SUBMISSION #: 8EHQ-0783-0485 S *

CAS NUMBER: 5915-41-3 CHEMICAL NAME: 1,3,5-TRIAZINE-2,4-DIAMINE, 6-CHLORO-N-(1,1-DIMETHYLETHYL)-N'-ETHYL-

SUBMISSION #: 8EHQ-0783-0485 S *

APPENDIX B: STATUS REPORTS BY CAS NUMBER (CONT.)

CAS NUMBER: 7550-45-0 CHEMICAL NAME: TITANIUM CHLORIDE (TICL4), (T-4)-
SUBMISSION #: 8EHQ-0984-0530

CAS NUMBER: 7647-01-0 CHEMICAL NAME: HYDROCHLORIC ACID
SUBMISSION #: 8EHQ-0384-0508 P *

CAS NUMBER: 7647-18-9 CHEMICAL NAME: ANTIMONY CHLORIDE (SBCL5)
SUBMISSION #: 8EHQ-0384-0508 P *

CAS NUMBER: 7664-39-3 CHEMICAL NAME: HYDROFLUORIC ACID
SUBMISSION #: 8EHQ-0384-0508 P *

CAS NUMBER: 7803-49-8 CHEMICAL NAME: HYDROXYLAMINE
SUBMISSION #: 8EHQ-0484-0513

CAS NUMBER: 8008-20-6 CHEMICAL NAME: KEROSINE
SUBMISSION #: 8EHQ-0283-0471 S 8EHQ-0283-0472 S

CAS NUMBER: 8052-41-3 CHEMICAL NAME: SOLVENT, STODDARD
SUBMISSION #: 8EHQ-0584-0517

CAS NUMBER: 8052-41-3 CHEMICAL NAME: STODDARD SOLVENT
SUBMISSION #: 8EHQ-0584-0517

CAS NUMBER: 9003-07-0 CHEMICAL NAME: POLYPROPYLENE
SUBMISSION #: 8EHQ-0583-0479 S

APPENDIX B: STATUS REPORTS BY CAS NUMBER (CONT.)

CAS NUMBER: 9003-07-0
SUBMISSION #: 8EHQ-0583-0479 S
CHEMICAL NAME: 1-PROPENE, HOMOPOLYMER

CAS NUMBER: 9003-11-6
SUBMISSION #: 8EHQ-0584-0516 S
CHEMICAL NAME: OXIRANE, METHYL-, POLYMER WITH OXIRANE

CAS NUMBER: 10039-54-0
SUBMISSION #: 8EHQ-0783-0486
CHEMICAL NAME: HYDROXYLAMINE, SULFATE (2:1) (SALT)

CAS NUMBER: 10212-58-5
SUBMISSION #: 8EHQ-1084-0535
CHEMICAL NAME: 1-AZIRIDINECARBOXAMIDE, 2-METHYL-N-OCTADECYL-

CAS NUMBER: 13463-67-7
SUBMISSION #: 8EHQ-1083-0497
CHEMICAL NAME: TITANIUM OXIDE (TIO2)

CAS NUMBER: 14567-73-8
SUBMISSION #: 8EHQ-0383-0473
CHEMICAL NAME: TREMOLITE

CAS NUMBER: 20328-87-4
SUBMISSION #: 8EHQ-0584-0519
CHEMICAL NAME: PINA SENSITIZER KF 501

CAS NUMBER: 20328-87-4
SUBMISSION #: 8EHQ-0584-0519
CHEMICAL NAME: 2-THIAZOLIUM, 2,2'-[(2-CARBOXY-P-PHENYLENE)BIS(IMINOVINYLENE)]BIS(3-ETHYL)DIIODIDE

APPENDIX B: STATUS REPORTS BY CAS NUMBER (CONT.)

CAS NUMBER: 20762-60-1 CHEMICAL NAME: POTASSIUM AZIDE (K(N3))
SUBMISSION #: 8EHQ-1083-0494 *

CAS NUMBER: 25068-38-6 CHEMICAL NAME: PHENOL, 4,4'-(1-METHYLETHYLIDENE)BIS-, POLYMER WITH (CHLOROMETHYL)OXIRANE
SUBMISSION #: 8EHQ-0584-0518 S

CAS NUMBER: 25167-67-3 CHEMICAL NAME: BUTENE
SUBMISSION #: 8EHQ-0484-0511

CAS NUMBER: 26544-23-0 CHEMICAL NAME: PHOSPHOROUS ACID, ISODECYL DIPHENYL ESTER
SUBMISSION #: 8EHQ-0784-0522

CAS NUMBER: 26628-22-8 CHEMICAL NAME: SODIUM AZIDE (NA(N3))
SUBMISSION #: 8EHQ-1083-0494 *

CAS NUMBER: 51200-87-4 CHEMICAL NAME: OXAZOLIDINE, 4,4-DIMETHYL-
SUBMISSION #: 8EHQ-0283-0470

CAS NUMBER: 51365-70-9 CHEMICAL NAME: EPON CURING AGENT D
SUBMISSION #: 8EHQ-0583-0478 S

CAS NUMBER: 51365-70-9 CHEMICAL NAME: HEXANOIC ACID, 2-ETHYL-, COMPD. WITH 2,4,6-TRIS[(DIMETHYLAMINO)METHYL]PHENOL
SUBMISSION #: 8EHQ-0583-0478 S

CAS NUMBER: 61791-44-4 CHEMICAL NAME: ETHANOL, 2,2'-IMINOBIS-, N-TALLOW ALKYL DERIVS.
SUBMISSION #: 8EHQ-0583-0479 S

CAS NUMBER: 63449-39-8 CHEMICAL NAME: CHLORINATED PARAFFINS
SUBMISSION #: 8EHQ-0983-0491 S 8EHQ-0484-0512 8EHQ-0884-0527

CAS NUMBER: 63449-39-8 CHEMICAL NAME: PARAFFIN WAXES AND HYDROCARBON WAXES, CHLORINATED
SUBMISSION #: 8EHQ-0983-0491 S 8EHQ-0484-0512 8EHQ-0884-0527

CAS NUMBER: 64741-53-3 CHEMICAL NAME: DISTILLATES (PETROLEUM), HEAVY NAPHTHENIC
SUBMISSION #: 8EHQ-0384-0507

CAS NUMBER: 64741-53-3 CHEMICAL NAME: GULF 100 TEXAS DISTILLATE
SUBMISSION #: 8EHQ-0384-0507

CAS NUMBER: 64741-59-9 CHEMICAL NAME: DISTILLATES (PETROLEUM), LIGHT CATALYTIC CRACKED
SUBMISSION #: 8EHQ-0183-0468

CAS NUMBER: 64741-60-2 CHEMICAL NAME: DISTILLATES (PETROLEUM), INTERMEDIATE CATALYTIC CRACKED
SUBMISSION #: 8EHQ-0183-0468

CAS NUMBER: 64741-61-3 CHEMICAL NAME: DISTILLATES (PETROLEUM), HEAVY CATALYTIC CRACKED
SUBMISSION #: 8EHQ-0183-0468

CAS NUMBER: 64741-62-4 CHEMICAL NAME: CLARIFIED OILS (PETROLEUM), CATALYTIC CRACKED
SUBMISSION #: 8EHQ-0584-0517

APPENDIX B: STATUS REPORTS BY CAS NUMBER (CONT.)

CAS NUMBER: 64741-68-0 CHEMICAL NAME: NAPHTHA (PETROLEUM), HEAVY CATALYTIC REFORMED
SUBMISSION #: 8EHQ-0283-0472 S

CAS NUMBER: 64741-88-4 CHEMICAL NAME: DISTILLATES (PETROLEUM), SOLVENT-REFINED HEAVY PARAFFINIC
SUBMISSION #: 8EHQ-0284-0505

CAS NUMBER: 64742-11-6 CHEMICAL NAME: EXTRACTS (PETROLEUM), HEAVY NAPHTHENIC DISTILLATE SOLVENT
SUBMISSION #: 8EHQ-0384-0507

CAS NUMBER: 64742-11-6 CHEMICAL NAME: GULF N.E. 61 (PROCESS 65)
SUBMISSION #: 8EHQ-0384-0507

CAS NUMBER: 64742-30-9 CHEMICAL NAME: DISTILLATES (PETROLEUM), CHEMICALLY NEUTRALIZED MIDDLE
SUBMISSION #: 8EHQ-0683-0480

CAS NUMBER: 64742-30-9 CHEMICAL NAME: MENTOR 28
SUBMISSION #: 8EHQ-0683-0480

CAS NUMBER: 64742-30-9 CHEMICAL NAME: SOMENTOR 43
SUBMISSION #: 8EHQ-0683-0480

CAS NUMBER: 64742-52-5 CHEMICAL NAME: DISTILLATES (PETROLEUM), HYDROTREATED HEAVY NAPHTHENIC
SUBMISSION #: 8EHQ-0384-0507

CAS NUMBER: 64742-52-5 CHEMICAL NAME: GULF 100 TEXAS OIL
SUBMISSION #: 8EHQ-0384-0507

APPENDIX B: STATUS REPORTS BY CAS NUMBER (CONT.)

CAS NUMBER: 64742-54-7 CHEMICAL NAME: DISTILLATES (PETROLEUM), HYDROTREATED HEAVY PARAFFINIC
SUBMISSION #: 8EHQ-0484-0512

CAS NUMBER: 64742-57-0 CHEMICAL NAME: RESIDUAL OILS (PETROLEUM), HYDROTREATED
SUBMISSION #: 8EHQ-0484-0512

CAS NUMBER: 64742-65-0 CHEMICAL NAME: DISTILLATES (PETROLEUM), SOLVENT-DEWAXED HEAVY PARAFFINIC
SUBMISSION #: 8EHQ-0284-0505

CAS NUMBER: 64742-90-1 CHEMICAL NAME: RESIDUES (PETROLEUM), STEAM-CRACKED
SUBMISSION #: 8EHQ-1083-0498

CAS NUMBER: 68131-74-8 CHEMICAL NAME: ASHES (RESIDUES)
SUBMISSION #: 8EHQ-0683-0482

CAS NUMBER: 68298-78-2 CHEMICAL NAME: PERFLUOROALKYL RESIN
SUBMISSION #: 8EHQ-1084-0535

CAS NUMBER: 68298-78-2 CHEMICAL NAME: 2-PROPENOIC ACID, 2-METHYL-, 2-[[[[5-[[[2-[ETHYL[(HEPTADECAF
LUOROOCTYL)SULFONYL]AMINO]ETHOXY]CARBONYL]AMINO]-2-METHYLPHE
NYL]AMINO]CARBONYL]OXY]PROPYL ESTER, TELOMER WITH BUTYL 2-PR
OPENOATE, 2-[[[[5-[[[2-[ETHYL[(NONAFLUOROBUTYL)SULFONYL]AMIN
O]ETHOXY]CARBONYL]AMINO]-2-METHYLPHENYL]AMINO]CARBONYL]OXY]P
SUBMISSION #: 8EHQ-1084-0535

CAS NUMBER: 68308-34-9 CHEMICAL NAME: SHALE OILS
SUBMISSION #: 8EHQ-0184-0504

APPENDIX B: STATUS REPORTS BY CAS NUMBER (CONT.)

CAS NUMBER: 68409-94-9 CHEMICAL NAME: FUEL, SRC SOLID
SUBMISSION #: 8EHQ-0683-0482

CAS NUMBER: 68409-94-9 CHEMICAL NAME: RESIDUES (COAL), SOLVENT-REFINING (SRC), VACUUM-DISTN.
SUBMISSION #: 8EHQ-0683-0482

CAS NUMBER: 68442-97-7 CHEMICAL NAME: 1H-IMIDAZOLE-1-ETHANAMINE, 4,5-DIHYDRO-, 2-NORTALL-OIL ALKYL DERIVS.
SUBMISSION #: 8EHQ-0984-0531 S *

CAS NUMBER: 68476-79-9 CHEMICAL NAME: NAPHTHA (COAL), SOLVENT-REFINING
SUBMISSION #: 8EHQ-0683-0482
CAS NUMBER: 68477-31-6 (See Below ***)
CAS NUMBER: 68479-98-1 CHEMICAL NAME: BENZENEDIAMINE, AR,AR-DIETHYL-AR-METHYL-
SUBMISSION #: 8EHQ-0883-0489

CAS NUMBER: 68555-92-0 CHEMICAL NAME: PERFLUOROALKYL RESIN
SUBMISSION #: 8EHQ-1084-0535

CAS NUMBER: 68555-92-0 CHEMICAL NAME: 2-PROPENOIC ACID, 2-METHYL-, 2-[[(HEPTADECAFLUOROOCTYL)SULFONYL]METHYLAMINO]ETHYL ESTER, POLYMER WITH 2-[METHYL[(NONAFLUOROBUTYL)SULFONYL]AMINO]ETHYL 2-METHYL-2-PROPENOATE, 2-[METHYL[(PENTADECAFLUOROHEPTYL)SULFONYL]AMINO]ETHYL 2-METHYL-2-PROPENOATE, 2-[METHYL[(TRIDECAFLUOROHEXYL)SULFONYL]AMINO]ETHYL
SUBMISSION #: 8EHQ-1084-0535

CAS NUMBER: 68911-57-9 CHEMICAL NAME: DISTILLATES (COAL), SOLVENT-REFINING (SRC), MIDDLE
SUBMISSION #: 8EHQ-0683-0482
CAS NUMBER: 68477-31-6 CHEMICAL NAME: DISTILLATES (PETROLEUM), CATALYTIC REFORMER FRACTIONATOR RESIDUE, LOW-BOILING
SUBMISSION #: 8EHQ-0283-0472 S

APPENDIX B: STATUS REPORTS BY CAS NUMBER (CONT.)

CAS NUMBER: 69013-21-4 CHEMICAL NAME: FUEL OILS, PYROLYSIS
SUBMISSION #: 8EHQ-1184-0537

CAS NUMBER: 69045-78-9 CHEMICAL NAME: PYRIDINE, 2-CHLORO-5-TRICHLOROMETHYL-
SUBMISSION #: 8EHQ-1084-0533 S

CAS NUMBER: 70776-26-0 CHEMICAL NAME: DISULFIDE, BIS(2-CHLOROOCTYL)
SUBMISSION #: 8EHQ-0283-0471 S

CAS NUMBER: 71868-10-5 CHEMICAL NAME: IRGACURE 907
SUBMISSION #: 8EHQ-0684-0520

CAS NUMBER: 71868-10-5 CHEMICAL NAME: 1-PROPANONE, 2-METHYL-1-[(4-METHYLTHIO)PHENYL]-2-(4-MORPHOLINYL)-
SUBMISSION #: 8EHQ-0684-0520

CAS NUMBER: 76379-66-3 CHEMICAL NAME: 5,7,11-DODECATRIYN-1-OL
SUBMISSION #: 8EHQ-1084-0532

CAS NUMBER: 77536-68-6 CHEMICAL NAME: TREMOLITE ASBESTOS
SUBMISSION #: 8EHQ-0383-0473

CAS NUMBER: 79419-43-5 CHEMICAL NAME: 2-CYCLOHEXEN-1-ONE, 2-(2-OXOBUTYL)-5-(2-ETHYLTHIO)-PROPYL-3-HYDROXY-
SUBMISSION #: 8EHQ-1283-0501

APPENDIX B: STATUS REPORTS BY CAS NUMBER (CONT.)

CAS NUMBER: 79419-43-5 CHEMICAL NAME: ORTHO 36015

SUBMISSION #: 8EHQ-1283-0501

Based on a preliminary evaluation, EPA believes that the submitted information did not warrant reporting pursuant to Section 8(e) of TSCA. In most cases, the submitter was requested to provide the basis for the company's contention that the information offered reasonable support for the conclusion that the subject chemical(s) posed a substantial risk of injury to health or the environment as defined in the Agency's March 16, 1978 Section 8(e) policy statement (see Appendix A of this volume).

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME

CAS NUMBER: 75-07-0 CHEMICAL NAME: ACETALDEHYDE
SUBMISSION #: 8EHQ-0383-0474

CAS NUMBER: 79-06-1 CHEMICAL NAME: ACRYLAMIDE
SUBMISSION #: 8EHQ-0783-0488

CAS NUMBER: CONFIDENT CHEMICAL NAME: ACRYLIC POLYMER
SUBMISSION #: 8EHQ-0683-0484 S

CAS NUMBER: 7647-18-9 CHEMICAL NAME: ANTIMONY CHLORIDE (SBCL5)
SUBMISSION #: 8EHQ-0384-0508 P *

CAS NUMBER: 2451-62-9 CHEMICAL NAME: ARALDITE PT-810
SUBMISSION #: 8EHQ-0883-0490

CAS NUMBER: CONFIDENT CHEMICAL NAME: AROMATICS, SUBSTITUTED
SUBMISSION #: 8EHQ-0583-0477 S

CAS NUMBER: 68131-74-8 CHEMICAL NAME: ASHES (RESIDUES)
SUBMISSION #: 8EHQ-0683-0482

CAS NUMBER: 10212-58-5 CHEMICAL NAME: 1-AZIRIDINECARBOXAMIDE, 2-METHYL-N-OCTADECYL-
SUBMISSION #: 8EHQ-1084-0535

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

CAS NUMBER: 62-53-3 CHEMICAL NAME: BENZENAMINE
SUBMISSION #: 8EHQ-0484-0513

CAS NUMBER: 100-65-2 CHEMICAL NAME: BENZENAMINE, N-HYDROXY-
SUBMISSION #: 8EHQ-0484-0513

CAS NUMBER: CONFIDENT CHEMICAL NAME: BENZENAMINE, SUBSTITUTED POLYGLYCIDYL
SUBMISSION #: 8EHQ-1283-0500 S

CAS NUMBER: 89-62-3 CHEMICAL NAME: BENZENAMINE, 4-METHYL-2-NITRO-
SUBMISSION #: 8EHQ-1083-0496

CAS NUMBER: 100-44-7 CHEMICAL NAME: BENZENE, (CHLOROMETHYL)-
SUBMISSION #: 8EHQ-0884-0523

CAS NUMBER: 68479-98-1 CHEMICAL NAME: BENZENEDIAMINE, AR,AR-DIETHYL-AR-METHYL-
SUBMISSION #: 8EHQ-0883-0489

CAS NUMBER: 98-95-3 CHEMICAL NAME: BENZENE, NITRO-
SUBMISSION #: 8EHQ-0484-0513

CAS NUMBER: 98-07-7 CHEMICAL NAME: BENZENE, (TRICHLOROMETHYL)-
SUBMISSION #: 8EHQ-0884-0523

CAS NUMBER: 87-66-1 CHEMICAL NAME: 1,2,3-BENZENETRIOL
SUBMISSION #: 8EHQ-1284-0539

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

CAS NUMBER: 98-82-8 CHEMICAL NAME: BENZENE, (1-METHYLETHYL)-
SUBMISSION #: 8EHQ-1184-0536

CAS NUMBER: 480-96-6 CHEMICAL NAME: BENZOFURAZAN, 1-OXIDE
SUBMISSION #: 8EHQ-1284-0541 S

CAS NUMBER: 98-88-4 CHEMICAL NAME: BENZOYL CHLORIDE
SUBMISSION #: 8EHQ-0884-0523

CAS NUMBER: 1336-36-3 CHEMICAL NAME: 1,1'-BIPHENYL, CHLORO DERIVS.
SUBMISSION #: 8EHQ-0784-0521 S

CAS NUMBER: 1134-36-7 CHEMICAL NAME: [1,1'-BIPHENYL]-4-OL, 3-AMINO-
SUBMISSION #: 8EHQ-1083-0495

CAS NUMBER: 106-99-0 CHEMICAL NAME: 1,3-BUTADIENE
SUBMISSION #: 8EHQ-0484-0511

CAS NUMBER: NONE CHEMICAL NAME: 1,3-BUTADIENE FEEDSTOCK
SUBMISSION #: 8EHQ-0484-0511

CAS NUMBER: 106-97-8 CHEMICAL NAME: BUTANE
SUBMISSION #: 8EHQ-0484-0511

CAS NUMBER: 106-98-9 CHEMICAL NAME: 1-BUTENE
SUBMISSION #: 8EHQ-0484-0511

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

CAS NUMBER: 25167-67-3 CHEMICAL NAME: BUTENE
SUBMISSION #: 8EHQ-0484-0511

CAS NUMBER: 2426-08-6 CHEMICAL NAME: BUTYL GLYCIDYL ETHER
SUBMISSION #: 8EHQ-0584-0518 S

CAS NUMBER: CONFIDENT CHEMICAL NAME: CARBAMATE, ALIPHATIC
SUBMISSION #: 8EHQ-0983-0492 S

CAS NUMBER: NONE CHEMICAL NAME: CARBON BLACK FEEDSTOCK
SUBMISSION #: 8EHQ-0183-0468

CAS NUMBER: 63449-39-8 CHEMICAL NAME: CHLORINATED PARAFFINS
SUBMISSION #: 8EHQ-0983-0491 S 8EHQ-0484-0512 8EHQ-0884-0527

CAS NUMBER: 64741-62-4 CHEMICAL NAME: CLARIFIED OILS (PETROLEUM), CATALYTIC CRACKED
SUBMISSION #: 8EHQ-0584-0517

CAS NUMBER: NONE CHEMICAL NAME: COAL, SOLVENT-REFINING (SRC) PROCESS/PRODUCTS
SUBMISSION #: 8EHQ-0683-0482 8EHQ-1284-0538

CAS NUMBER: NONE CHEMICAL NAME: CONFIDENTIAL
SUBMISSION #: 8EHQ-0583-0479 S

CAS NUMBER: CONFIDENT CHEMICAL NAME: CONFIDENTIAL
SUBMISSION #: 8EHQ-0683-0483 S

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

CAS NUMBER: 98-82-8 CHEMICAL NAME: CUMENE
SUBMISSION #: 8EHQ-1184-0536

CAS NUMBER: NONE CHEMICAL NAME: CUTTING FLUID
SUBMISSION #: 8EHQ-0283-0469 S
8EHQ-0283-0471 S

CAS NUMBER: 79419-43-5 CHEMICAL NAME: 2-CYCLOHEXEN-1-ONE, 2-(2-OXOBUTYL)-5-(2-ETHYLTHIO)-PROPYL-3-HYDROXY-
SUBMISSION #: 8EHQ-1283-0501

CAS NUMBER: 103-33-3 CHEMICAL NAME: DIAZENE, DIPHENYL-
SUBMISSION #: 8EHQ-0484-0513

CAS NUMBER: 495-48-7 CHEMICAL NAME: DIAZENE, DIPHENYL-, 1-OXIDE
SUBMISSION #: 8EHQ-0484-0513

CAS NUMBER: 68911-57-9 CHEMICAL NAME: DISTILLATES (COAL), SOLVENT-REFINING (SRC), MIDDLE
SUBMISSION #: 8EHQ-0683-0482

CAS NUMBER: UNKNOWN CHEMICAL NAME: DISTILLATES (COAL), SOLVENT-REFINING (SRC), MIDDLE, TWO STAGE LIQUEFACTION (TSL)
SUBMISSION #: 8EHQ-0683-0482

CAS NUMBER: 64742-30-9 CHEMICAL NAME: DISTILLATES (PETROLEUM), CHEMICALLY NEUTRALIZED MIDDLE
SUBMISSION #: 8EHQ-0683-0480

CAS NUMBER: 68477-31-6 CHEMICAL NAME: DISTILLATES (PETROLEUM), CATALYTIC REFORMER FRACTIONATOR RESIDUE, LOW-BOILING
SUBMISSION #: 8EHQ-0283-0472 S

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

CAS NUMBER: 64741-61-3 CHEMICAL NAME: DISTILLATES (PETROLEUM), HEAVY CATALYTIC CRACKED
SUBMISSION #: 8EHQ-0183-0468

CAS NUMBER: 64741-53-3 CHEMICAL NAME: DISTILLATES (PETROLEUM), HEAVY NAPHTHENIC
SUBMISSION #: 8EHQ-0384-0507

CAS NUMBER: 64742-52-5 CHEMICAL NAME: DISTILLATES (PETROLEUM), HYDROTREATED HEAVY NAPHTHENIC
SUBMISSION #: 8EHQ-0384-0507

CAS NUMBER: 64742-54-7 CHEMICAL NAME: DISTILLATES (PETROLEUM), HYDROTREATED HEAVY PARAFFINIC
SUBMISSION #: 8EHQ-0484-0512

CAS NUMBER: 64741-60-2 CHEMICAL NAME: DISTILLATES (PETROLEUM), INTERMEDIATE CATALYTIC CRACKED
SUBMISSION #: 8EHQ-0183-0468

CAS NUMBER: 64741-59-9 CHEMICAL NAME: DISTILLATES (PETROLEUM), LIGHT CATALYTIC CRACKED
SUBMISSION #: 8EHQ-0183-0468

CAS NUMBER: 64742-65-0 CHEMICAL NAME: DISTILLATES (PETROLEUM), SOLVENT-DEWAXED HEAVY PARAFFINIC
SUBMISSION #: 8EHQ-0284-0505

CAS NUMBER: 64741-88-4 CHEMICAL NAME: DISTILLATES (PETROLEUM), SOLVENT-REFINED HEAVY PARAFFINIC
SUBMISSION #: 8EHQ-0284-0505

CAS NUMBER: 70776-26-0 CHEMICAL NAME: DISULFIDE, BIS(2-CHLOROOCTYL)
SUBMISSION #: 8EHQ-0283-0471 S

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

CAS NUMBER: 76379-66-3 CHEMICAL NAME: 5,7,11-DODECATRIYN-1-OL
SUBMISSION #: 8EHQ-1084-0532

CAS NUMBER: UNKNOWN CHEMICAL NAME: DUST, SRC SOLID
SUBMISSION #: 8EHQ-1284-0538

CAS NUMBER: 106-89-8 CHEMICAL NAME: EPICHLOROHYDRIN
SUBMISSION #: 8EHQ-0584-0518 S

CAS NUMBER: 51365-70-9 CHEMICAL NAME: EPON CURING AGENT D
SUBMISSION #: 8EHQ-0583-0478 S

CAS NUMBER: NONE CHEMICAL NAME: EPON 815
SUBMISSION #: 8EHQ-0584-0518 S

CAS NUMBER: NONE CHEMICAL NAME: EPOXY RESINS
SUBMISSION #: 8EHQ-0883-0490
8EHQ-0584-0518 S 8EHQ-0584-0515 S 8EHQ-0584-0516 S

CAS NUMBER: 540-63-6 CHEMICAL NAME: 1,2-ETHANEDITHIOL
SUBMISSION #: 8EHQ-0683-0481

CAS NUMBER: 71-55-6 CHEMICAL NAME: ETHANE, 1,1,1-TRICHLORO-
SUBMISSION #: 8EHQ-1084-0535

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

CAS NUMBER: 76-13-1 CHEMICAL NAME: ETHANE, 1,1,2-TRICHLORO-1,2,2-TRIFLUORO-
SUBMISSION #: 8EHQ-1084-0535

CAS NUMBER: 111-76-2 CHEMICAL NAME: ETHANOL, 2-BUTOXY-
SUBMISSION #: 8EHQ-0483-0475
8EHQ-0584-0517

CAS NUMBER: 122-99-6 CHEMICAL NAME: ETHANOL, 2-PHENOXY-
SUBMISSION #: 8EHQ-0884-0528

CAS NUMBER: 61791-44-4 CHEMICAL NAME: ETHANOL, 2,2'-IMINOBIS-, N-TALLOW ALKYL DERIVS.
SUBMISSION #: 8EHQ-0583-0479 S

CAS NUMBER: 1116-54-7 CHEMICAL NAME: ETHANOL, 2,2'-(NITROSOIMINO)BIS-
SUBMISSION #: 8EHQ-0283-0469 S

CAS NUMBER: 64742-11-6 CHEMICAL NAME: EXTRACTS (PETROLEUM), HEAVY NAPHTHENIC DISTILLATE SOLVENT
SUBMISSION #: 8EHQ-0384-0507

CAS NUMBER: 50-00-0 CHEMICAL NAME: FORMALDEHYDE
SUBMISSION #: 8EHQ-0383-0474

CAS NUMBER: 76-13-1 CHEMICAL NAME: FREON 113
SUBMISSION #: 8EHQ-1084-0535

CAS NUMBER: UNKNOWN CHEMICAL NAME: FUEL OIL, LIGHT PYROLYSIS
SUBMISSION #: 8EHQ-1184-0537

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

CAS NUMBER: 69013-21-4 CHEMICAL NAME: FUEL OILS, PYROLYSIS
SUBMISSION #: 8EHQ-1184-0537

CAS NUMBER: 68409-94-9 CHEMICAL NAME: FUEL, SRC SOLID
SUBMISSION #: 8EHQ-0683-0482

CAS NUMBER: UNKNOWN CHEMICAL NAME: FUEL, TSL SOLID
SUBMISSION #: 8EHQ-0683-0482

CAS NUMBER: NONE CHEMICAL NAME: GREASE, GULFCROWN E.P. NO. 2
SUBMISSION #: 8EHQ-0484-0512

CAS NUMBER: NONE CHEMICAL NAME: GULFCROWN GREASE E.P. NO. 2
SUBMISSION #: 8EHQ-0484-0512

CAS NUMBER: 64742-11-6 CHEMICAL NAME: GULF N.E. 61 (PROCESS 65)
SUBMISSION #: 8EHQ-0384-0507

CAS NUMBER: 64741-53-3 CHEMICAL NAME: GULF 100 TEXAS DISTILLATE
SUBMISSION #: 8EHQ-0384-0507

CAS NUMBER: 64742-52-5 CHEMICAL NAME: GULF 100 TEXAS OIL
SUBMISSION #: 8EHQ-0384-0507

CAS NUMBER: 111-14-8 CHEMICAL NAME: HEPTANOIC ACID
SUBMISSION #: 8EHQ-0584-0514

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

CAS NUMBER: 111-07-9 CHEMICAL NAME: HEXADECANOIC ACID, 2-METHOXYETHYL ESTER
SUBMISSION #: 8EHQ-1084-0534

CAS NUMBER: 51365-70-9 CHEMICAL NAME: HEXANOIC ACID, 2-ETHYL-, COMPD. WITH 2,4,6-TRIS[(DIMETHYLAMINO)METHYL]PHENOL
SUBMISSION #: 8EHQ-0583-0478 S

CAS NUMBER: 7647-01-0 CHEMICAL NAME: HYDROCHLORIC ACID
SUBMISSION #: 8EHQ-0384-0508 P *

CAS NUMBER: 7664-39-3 CHEMICAL NAME: HYDROFLUORIC ACID
SUBMISSION #: 8EHQ-0384-0508 P *

CAS NUMBER: 7803-49-8 CHEMICAL NAME: HYDROXYLAMINE
SUBMISSION #: 8EHQ-0484-0513

CAS NUMBER: 10039-54-0 CHEMICAL NAME: HYDROXYLAMINE, SULFATE (2:1) (SALT)
SUBMISSION #: 8EHQ-0783-0486

CAS NUMBER: NONE CHEMICAL NAME: HYPALON MOLDING COMPOUND (THERMAL-DECOMPOSITION PRODUCTS)
SUBMISSION #: 8EHQ-1283-0502 P *

CAS NUMBER: 288-32-4 CHEMICAL NAME: 1H-IMIDAZOLE
SUBMISSION #: 8EHQ-1284-0540 S *

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

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CAS NUMBER:  68442-97-7                 CHEMICAL NAME: 1H-IMIDAZOLE-1-ETHANAMINE, 4,5-DIHYDRO-, 2-NORTALL-OIL ALKYL
                                                        DERIVS.
          SUBMISSION #: 8EHQ-0984-0531 S  *

CAS NUMBER:  931-36-2                   CHEMICAL NAME: 1H-IMIDAZOLE, 2-ETHYL-4-METHYL-
          SUBMISSION #: 8EHQ-1284-0540 S  *

CAS NUMBER:  71868-10-5                 CHEMICAL NAME: IRGACURE 907
          SUBMISSION #: 8EHQ-0684-0520

CAS NUMBER:  NONE                       CHEMICAL NAME: JP-8
          SUBMISSION #: 8EHQ-0283-0471 S

CAS NUMBER:  8008-20-6                  CHEMICAL NAME: KEROSINE
          SUBMISSION #: 8EHQ-0283-0471 S                 8EHQ-0283-0472 S

CAS NUMBER:  NONE                       CHEMICAL NAME: KLARUS 1717
          SUBMISSION #: 8EHQ-0283-0471 S

CAS NUMBER:  3033-77-0                  CHEMICAL NAME: G-MAC
          SUBMISSION #: 8EHQ-1283-0503

CAS NUMBER:  64742-30-9                 CHEMICAL NAME: MENTOR 28
          SUBMISSION #: 8EHQ-0683-0480
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APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

CAS NUMBER: 74-87-3 CHEMICAL NAME: METHANE, CHLORO-
SUBMISSION #: 8EHQ-1083-0499

CAS NUMBER: 75-09-2 CHEMICAL NAME: METHANE, DICHLORO-
SUBMISSION #: 8EHQ-0884-0525

CAS NUMBER: 67-56-1 CHEMICAL NAME: METHANOL
SUBMISSION #: 8EHQ-0484-0513

CAS NUMBER: 1143-72-2 CHEMICAL NAME: METHANONE, PHENYL(2,3,4-TRIHYDROXYPHENYL)-
SUBMISSION #: 8EHQ-0484-0510

CAS NUMBER: 75-09-2 CHEMICAL NAME: METHYLENE CHLORIDE
SUBMISSION #: 8EHQ-0884-0525

CAS NUMBER: NONE CHEMICAL NAME: MISC. CHEMICALS
SUBMISSION #: 8EHQ-1283-0502 P * 8EHQ-0384-0508 P *

CAS NUMBER: 68476-79-9 CHEMICAL NAME: NAPHTHA (COAL), SOLVENT-REFINING
SUBMISSION #: 8EHQ-0683-0482

CAS NUMBER: 64741-68-0 CHEMICAL NAME: NAPHTHA (PETROLEUM), HEAVY CATALYTIC REFORMED
SUBMISSION #: 8EHQ-0283-0472 S

CAS NUMBER: UNKNOWN CHEMICAL NAME: NICOTINIC ACID DERIVATIVE
SUBMISSION #: 8EHQ-0783-0487 S *

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

CAS NUMBER: NONE CHEMICAL NAME: NITROSAMINES
SUBMISSION #: 8EHQ-0283-0469 S

CAS NUMBER: 1116-54-7 CHEMICAL NAME: N-NITROSODIETHANOLAMINE
SUBMISSION #: 8EHQ-0283-0469 S

CAS NUMBER: 112-05-0 CHEMICAL NAME: NONANOIC ACID
SUBMISSION #: 8EHQ-0584-0514

CAS NUMBER: UNKNOWN CHEMICAL NAME: OIL (SHALE), LURGI LIGHT/MIDDLE
SUBMISSION #: 8EHQ-0184-0504

CAS NUMBER: UNKNOWN CHEMICAL NAME: OIL, UNSATURATED ALIPHATIC (C16-C32)
SUBMISSION #: 8EHQ-0884-0526

CAS NUMBER: 79419-43-5 CHEMICAL NAME: ORTHO 36015
SUBMISSION #: 8EHQ-1283-0501

CAS NUMBER: 2386-87-0 CHEMICAL NAME: 7-OXABICYCLO[4.1.0]HEPTANE-3-CARBOXYLIC ACID, 7-OXABICYCLO[4.1.0]HEPT-3-YLMETHYL ESTER
SUBMISSION #: 8EHQ-0784-0522

CAS NUMBER: 51200-87-4 CHEMICAL NAME: OXAZOLIDINE, 4,4-DIMETHYL-
SUBMISSION #: 8EHQ-0283-0470

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

CAS NUMBER: CONFIDENT CHEMICAL NAME: OXIDES, METALLIC (MIXTURE)
SUBMISSION #: 8EHQ-0983-0493 S *

CAS NUMBER: CONFIDENT CHEMICAL NAME: OXIDIZED WAX ACIDS, CALCIUM SOAP
SUBMISSION #: 8EHQ-0584-0517

CAS NUMBER: 2426-08-6 CHEMICAL NAME: OXIRANE, (BUTOXYMETHYL)-
SUBMISSION #: 8EHQ-0584-0518 S

CAS NUMBER: 106-89-8 CHEMICAL NAME: OXIRANE, (CHLOROMETHYL)-
SUBMISSION #: 8EHQ-0584-0518 S

CAS NUMBER: 3033-77-0 CHEMICAL NAME: OXIRANEMETHANAMINIUM, N,N,N-TRIMETHYL-, CHLORIDE
SUBMISSION #: 8EHQ-1283-0503

CAS NUMBER: 9003-11-6 CHEMICAL NAME: OXIRANE, METHYL-, POLYMER WITH OXIRANE
SUBMISSION #: 8EHQ-0584-0516 S

CAS NUMBER: 63449-39-8 CHEMICAL NAME: PARAFFIN WAXES AND HYDROCARBON WAXES, CHLORINATED
SUBMISSION #: 8EHQ-0983-0491 S 8EHQ-0484-0512 8EHQ-0884-0527

CAS NUMBER: 109-52-4 CHEMICAL NAME: PENTANOIC ACID
SUBMISSION #: 8EHQ-0584-0514

CAS NUMBER: 108-10-1 CHEMICAL NAME: 2-PENTANONE, 4-METHYL-
SUBMISSION #: 8EHQ-1084-0535

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

CAS NUMBER: NONE CHEMICAL NAME: PERFLUOROALKYL COMPOUNDS
SUBMISSION #: 8EHQ-1084-0535

CAS NUMBER: 68298-78-2/ CHEMICAL NAME: PERFLUOROALKYL RESIN
SUBMISSION #: 8EHQ-1084-0535

CAS NUMBER: 68555-92-0 CHEMICAL NAME: PERFLUOROALKYL RESIN
SUBMISSION #: 8EHQ-1084-0535

CAS NUMBER: CONFIDENT CHEMICAL NAME: PETROLEUM SULFONATE, CALCIUM
SUBMISSION #: 8EHQ-0584-0517

CAS NUMBER: 92-43-3 CHEMICAL NAME: PHENIDONE
SUBMISSION #: 8EHQ-0984-0529

CAS NUMBER: 123-30-8 CHEMICAL NAME: PHENOL, 4-AMINO-
SUBMISSION #: 8EHQ-0484-0513

CAS NUMBER: 51-78-5 CHEMICAL NAME: PHENOL, 4-AMINO-, HYDROCHLORIDE
SUBMISSION #: 8EHQ-0484-0513

CAS NUMBER: 25068-38-6 CHEMICAL NAME: PHENOL, 4,4'-(1-METHYLETHYLIDENE)BIS-, POLYMER WITH (CHLOROM
ETHYL)OXIRANE
SUBMISSION #: 8EHQ-0584-0518 S

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

CAS NUMBER: 1429-50-1 CHEMICAL NAME: PHOSPHONIC ACID, [1,2-ETHANEDIYLBIS[NITRILOBIS(METHYLENE)]]TETRAKIS-
SUBMISSION #: 8EHQ-0683-0483 S

CAS NUMBER: 26544-23-0 CHEMICAL NAME: PHOSPHOROUS ACID, ISODECYL DIPHENYL ESTER
SUBMISSION #: 8EHQ-0784-0522

CAS NUMBER: 20328-87-4 CHEMICAL NAME: PINA SENSITIZER KF 501
SUBMISSION #: 8EHQ-0584-0519

CAS NUMBER: 1336-36-3 CHEMICAL NAME: POLYCHLORINATED BIPHENYLS (PCB)
SUBMISSION #: 8EHQ-0784-0521 S

CAS NUMBER: 9003-07-0 CHEMICAL NAME: POLYPROPYLENE
SUBMISSION #: 8EHQ-0583-0479 S

CAS NUMBER: 20762-60-1 CHEMICAL NAME: POTASSIUM AZIDE (K(N3))
SUBMISSION #: 8EHQ-1083-0494 *

CAS NUMBER: 3327-22-8 CHEMICAL NAME: 1-PROPANAMINIUM, 3-CHLORO-2-HYDROXY-N,N,N-TRIMETHYL-, CHLORIDE
SUBMISSION #: 8EHQ-1283-0503

CAS NUMBER: 75-28-5 CHEMICAL NAME: PROPANE, 2-METHYL-
SUBMISSION #: 8EHQ-0484-0511

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

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CAS NUMBER:  71868-10-5                  CHEMICAL NAME: 1-PROPANONE, 2-METHYL-1-[(4-METHYLTHIO)PHENYL]-2-(4-MORPHOLI
                                                        NYL)-
         SUBMISSION #: 8EHQ-0684-0520

CAS NUMBER:  79-06-1                     CHEMICAL NAME: 2-PROPENAMIDE
         SUBMISSION #: 8EHQ-0783-0488

CAS NUMBER:  9003-07-0                   CHEMICAL NAME: 1-PROPENE, HOMOPOLYMER
         SUBMISSION #: 8EHQ-0583-0479 S

CAS NUMBER:  115-11-7                    CHEMICAL NAME: 1-PROPENE, 2-METHYL-
         SUBMISSION #: 8EHQ-0484-0511

CAS NUMBER:  382-10-5                    CHEMICAL NAME: 1-PROPENE, 3,3,3-TRIFLUORO-2-(TRIFLUOROMETHYL)-
         SUBMISSION #: 8EHQ-0483-0476 S

CAS NUMBER:  68555-92-0                  CHEMICAL NAME: 2-PROPENOIC ACID, 2-METHYL-, 2-[[(HEPTADECAFLUOROOCTYL)SULFO
                                                        NYL]METHYLAMINO]ETHYL ESTER, POLYMER WITH 2-[METHYL[(NONAFLU
                                                        OROBUTYL)SULFONYL]AMINO]ETHYL 2-METHYL-2-PROPENOATE, 2-[METH
                                                        YL[(PENTADECAFLUOROHEPTYL)SULFONYL]AMINO]ETHYL 2-METHYL-2-PR
         SUBMISSION #: 8EHQ-1084-0535                   OPENOATE, 2-[METHYL[(TRIDECAFLUOROHEXYL)SULFONYL]AMINO]ETHYL

CAS NUMBER:  68298-78-2                  CHEMICAL NAME: 2-PROPENOIC ACID, 2-METHYL-, 2-[[[[5-[[[2-[ETHYL[(HEPTADECAF
                                                        LUOROOCTYL)SULFONYL]AMINO]ETHOXY]CARBONYL]AMINO]-2-METHYLPHE
                                                        NYL]AMINO]CARBONYL]OXY]PROPYL ESTER, TELOMER WITH BUTYL 2-PR
                                                        OPENOATE, 2-[[[[5-[[[2-[ETHYL[(NONAFLUOROBUTYL)SULFONYL]AMIN
         SUBMISSION #: 8EHQ-1084-0535                   O]ETHOXY]CARBONYL]AMINO]-2-METHYLPHENYL]AMINO]CARBONYL]OXY]P
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APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

CAS NUMBER: 2530-85-0 CHEMICAL NAME: 2-PROPENOIC ACID, 2-METHYL-, 3-(TRIMETHOXYSILYL)PROPYL ESTER
SUBMISSION #: 8EHQ-0884-0524

CAS NUMBER: 92-43-3 CHEMICAL NAME: 3-PYRAZOLIDINONE, 1-PHENYL-
SUBMISSION #: 8EHQ-0984-0529

CAS NUMBER: 69045-78-9 CHEMICAL NAME: PYRIDINE, 2-CHLORO-5-TRICHLOROMETHYL-
SUBMISSION #: 8EHQ-1084-0533 S

CAS NUMBER: 87-66-1 CHEMICAL NAME: PYROGALLOL
SUBMISSION #: 8EHQ-1284-0539

CAS NUMBER: 64742-57-0 CHEMICAL NAME: RESIDUAL OILS (PETROLEUM), HYDROTREATED
SUBMISSION #: 8EHQ-0484-0512

CAS NUMBER: 68409-94-9 CHEMICAL NAME: RESIDUES (COAL), SOLVENT-REFINING (SRC), VACUUM-DISTN.
SUBMISSION #: 8EHQ-0683-0482

CAS NUMBER: UNKNOWN CHEMICAL NAME: RESIDUES (COAL), SOLVENT-REFINING (SRC), VACUUM-DISTN., TWO STAGE LIQUEFACTION (TSL)
SUBMISSION #: 8EHQ-0683-0482

CAS NUMBER: 64742-90-1 CHEMICAL NAME: RESIDUES (PETROLEUM), STEAM-CRACKED
SUBMISSION #: 8EHQ-1083-0498

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

CAS NUMBER: NONE CHEMICAL NAME: RUST-BAN 392
SUBMISSION #: 8EHQ-0584-0517

CAS NUMBER: 68308-34-9 CHEMICAL NAME: SHALE OILS
SUBMISSION #: 8EHQ-0184-0504

CAS NUMBER: 2530-85-0 CHEMICAL NAME: SILANE A-174
SUBMISSION #: 8EHQ-0884-0524

CAS NUMBER: 26628-22-8 CHEMICAL NAME: SODIUM AZIDE (NA(N3))
SUBMISSION #: 8EHQ-1083-0494 *

CAS NUMBER: 8052-41-3 CHEMICAL NAME: SOLVENT, STODDARD
SUBMISSION #: 8EHQ-0584-0517

CAS NUMBER: 64742-30-9 CHEMICAL NAME: SOMENTOR 43
SUBMISSION #: 8EHQ-0683-0480

CAS NUMBER: NONE CHEMICAL NAME: SRC PROCESS/PRODUCTS
SUBMISSION #: 8EHQ-0683-0482 8EHQ-1284-0538

CAS NUMBER: 8052-41-3 CHEMICAL NAME: STODDARD SOLVENT
SUBMISSION #: 8EHQ-0584-0517

CAS NUMBER: 64-67-5 CHEMICAL NAME: SULFURIC ACID, DIETHYL ESTER
SUBMISSION #: 8EHQ-1083-0509

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

CAS NUMBER: 5915-41-3 CHEMICAL NAME: TERBUTHYLAZINE
SUBMISSION #: 8EHQ-0783-0485 S *

CAS NUMBER: 20328-87-4 CHEMICAL NAME: 2-THIAZOLIUM, 2,2'-[(2-CARBOXY-P-PHENYLENE)BIS(IMINOVINYLENE)]BIS(3-ETHYL)DIIODIDE
SUBMISSION #: 8EHQ-0584-0519

CAS NUMBER: UNKNOWN CHEMICAL NAME: 2-THIAZOLIUM, 2,2'-[(2-CARBOXY-P-PHENYLENE)BIS(IMINOVINYLENE)]BIS(3-ETHYL)DIIODIDE, TRIETHYLAMINE SALT
SUBMISSION #: 8EHQ-0584-0519

CAS NUMBER: 7550-45-0 CHEMICAL NAME: TITANIUM CHLORIDE (TICL4), (T-4)-
SUBMISSION #: 8EHQ-0984-0530

CAS NUMBER: 13463-67-7 CHEMICAL NAME: TITANIUM OXIDE (TIO2)
SUBMISSION #: 8EHQ-1083-0497

CAS NUMBER: 14567-73-8 CHEMICAL NAME: TREMOLITE
SUBMISSION #: 8EHQ-0383-0473

CAS NUMBER: 77536-68-6 CHEMICAL NAME: TREMOLITE ASBESTOS
SUBMISSION #: 8EHQ-0383-0473

CAS NUMBER: 959-52-4 CHEMICAL NAME: 1,3,5-TRIAZINE, HEXAHYDRO-1,3,5-TRIS(1-OXO-2-PROPENYL)-
SUBMISSION #: 8EHQ-0384-0506 S

APPENDIX C: STATUS REPORTS BY CHEMICAL NAME (CONT.)

CAS NUMBER: 5915-41-3 CHEMICAL NAME: 1,3,5-TRIAZINE-2,4-DIAMINE, 6-CHLORO-N-(1,1-DIMETHYLETHYL)-N'-ETHYL-
SUBMISSION #: 8EHQ-0783-0485 S *

CAS NUMBER: 2451-62-9 CHEMICAL NAME: 1,3,5-TRIAZINE-2,4,6(1H,3H,5H)-TRIONE, 1,3,5-TRIS(OXIRANYLMETHYL)-
SUBMISSION #: 8EHQ-0883-0490

CAS NUMBER: 1318-00-9 CHEMICAL NAME: VERMICULITE
SUBMISSION #: 8EHQ-0383-0473

CAS NUMBER: NONE CHEMICAL NAME: ZINC DIALKYL DITHIOPHOSPHATES (ZDDP)
SUBMISSION #: 8EHQ-0484-0512

CAS NUMBER: UNKNOWN CHEMICAL NAME: ZINC DIAMYL DITHIOCARBAMATES
SUBMISSION #: 8EHQ-0484-0512

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* Based on a preliminary evaluation, EPA believes that the submitted information did not warrant reporting pursuant to Section 8(e) of TSCA. In most cases, the submitter was requested to provide the basis for the company's contention that the information offered reasonable support for the conclusion that the subject chemical(s) posed a substantial risk of injury to health or the environment as defined in the Agency's March 16, 1978 Section 8(e) policy statement (see Appendix A of this volume).

APPENDIX D: STATUS REPORTS BY INFORMATION TYPE

ACUTE TOXICITY (ANIMAL)

SUBMISSION #:
8EHQ-0183-0468
8EHQ-0283-0471 S
8EHQ-0483-0476 S
8EHQ-0583-0478 S
8EHQ-0583-0479 S
8EHQ-0683-0482
8EHQ-0783-0485 S *
8EHQ-0783-0486
8EHQ-0783-0487 S *
8EHQ-0883-0490
8EHQ-0983-0492 S
8EHQ-1083-0494 *
8EHQ-1083-0495
8EHQ-1083-0496
8EHQ-1083-0497
8EHQ-1283-0501
8EHQ-0484-0510
8EHQ-0484-0513
8EHQ-0584-0519
8EHQ-0884-0528
8EHQ-0984-0530
8EHQ-0984-0531 S *
8EHQ-1084-0532
8EHQ-1084-0535
8EHQ-1284-0540 S *

ACUTE TOXICITY (HUMAN)

SUBMISSION #:
8EHQ-0283-0471 S
8EHQ-0783-0486
8EHQ-0983-0493 S *
8EHQ-1283-0502 P *
8EHQ-0384-0508 P *
8EHQ-0484-0513
8EHQ-0984-0529
8EHQ-1084-0532
8EHQ-1084-0535

ALLERGENICITY (ANIMAL)

SUBMISSION #:
8EHQ-0283-0471 S
8EHQ-0683-0482
8EHQ-0783-0486
8EHQ-0883-0490
8EHQ-1083-0495
8EHQ-1084-0532

ALLERGENICITY (HUMAN)

SUBMISSION #:
8EHQ-0283-0471 S
8EHQ-1084-0532

CELL TRANSFORMATION (IN VITRO)

SUBMISSION #:
8EHQ-0583-0477 S
8EHQ-0883-0490
8EHQ-1083-0495

APPENDIX D: STATUS REPORTS BY INFORMATION TYPE (CONT.)

CELL TRANSFORMATION (IN VITRO) (CONT.)

SUBMISSION #:			
	8EHQ-1083-0496	8EHQ-1083-0498	8EHQ-0484-0511
	8EHQ-0484-0512	8EHQ-0584-0516 S	8EHQ-1184-0536
	8EHQ-1184-0537		

CHEMICAL/PHYSICAL PROPERTIES

SUBMISSION #:			
	8EHQ-0483-0475	8EHQ-0583-0478 S	8EHQ-0583-0479 S
	8EHQ-0683-0480	8EHQ-0683-0481	8EHQ-0683-0482
	8EHQ-0683-0484 S	8EHQ-0783-0486	8EHQ-0883-0490
	8EHQ-0983-0491 S	8EHQ-0983-0492 S	8EHQ-1083-0495
	8EHQ-1083-0496	8EHQ-1083-0498	8EHQ-1283-0501
	8EHQ-1283-0502 P *	8EHQ-1283-0503	8EHQ-1083-0509
	8EHQ-0484-0513	8EHQ-0584-0519	8EHQ-0684-0520
	8EHQ-0784-0522	8EHQ-0984-0530	8EHQ-1084-0534

CHRONIC TOXICITY (ANIMAL)

SUBMISSION #:			
	8EHQ-0283-0469 S	8EHQ-0283-0472 S	8EHQ-0383-0474
	8EHQ-0683-0480	8EHQ-0683-0483 S	8EHQ-0783-0488
	8EHQ-1083-0497	8EHQ-1283-0503	8EHQ-1083-0509
	8EHQ-0584-0514	8EHQ-0584-0517	8EHQ-0884-0525
	8EHQ-0884-0526	8EHQ-0984-0530	8EHQ-1284-0538

CHRONIC TOXICITY (HUMAN)

SUBMISSION #:		
	8EHQ-0383-0473	8EHQ-0884-0523

APPENDIX D: STATUS REPORTS BY INFORMATION TYPE (CONT.)

CLASTOGENICITY (ANIMAL)

SUBMISSION #:	8EHQ-0483-0476 S	8EHQ-0583-0477 S	8EHQ-0883-0490
	8EHQ-0384-0506 S	8EHQ-0484-0511	8EHQ-0484-0512
	8EHQ-1184-0537		

CLASTOGENICITY (IN VITRO)

SUBMISSION #:	8EHQ-0683-0481	8EHQ-1283-0500 S	8EHQ-0384-0506 S
	8EHQ-1083-0509	8EHQ-0484-0510	8EHQ-0584-0515 S
	8EHQ-0584-0516 S	8EHQ-0584-0518 S	8EHQ-0784-0522
	8EHQ-1084-0533 S	8EHQ-1284-0539	

DNA DAMAGE/REPAIR

SUBMISSION #:	8EHQ-0583-0477 S	8EHQ-0683-0481	8EHQ-1283-0503
	8EHQ-0384-0506 S	8EHQ-1083-0509	8EHQ-0484-0511
	8EHQ-0484-0512	8EHQ-1184-0536	8EHQ-1184-0537

ECOTOXICITY/AQUATIC TOXICITY

SUBMISSION #:	8EHQ-0783-0486	8EHQ-0983-0491 S	8EHQ-1083-0495

ENV. OCCURRENCE/RELEASE/FATE

SUBMISSION #:	8EHQ-0983-0491 S	8EHQ-1083-0495	8EHQ-0384-0508 P *
	8EHQ-0784-0521 S		

EPIDEMIOLOGY/CLINICAL

SUBMISSION #:	8EHQ-0383-0473	8EHQ-1083-0497	8EHQ-0884-0523

APPENDIX D: STATUS REPORTS BY INFORMATION TYPE (CONT.)

HUMAN EXPOSURE (ACCIDENTAL)

SUBMISSION #: 8EHQ-0384-0508 P * 8EHQ-0484-0513

HUMAN EXPOSURE (MONITORING)

SUBMISSION #: 8EHQ-0383-0473 8EHQ-1083-0495 8EHQ-1083-0497
8EHQ-0184-0504 8EHQ-0784-0521 S 8EHQ-1084-0535

HUMAN EXPOSURE (PRODUCT CONTAMINATION)

SUBMISSION #: 8EHQ-0283-0469 S 8EHQ-0383-0473 8EHQ-0784-0521 S

METABOLISM/PHARMACOKINETICS (ANIMAL)

SUBMISSION #: 8EHQ-0983-0491 S

METABOLISM/PHARMACOKINETICS (HUMAN)

SUBMISSION #: 8EHQ-0484-0513

MUTAGENICITY (IN VITRO)

SUBMISSION #: 8EHQ-0183-0468 8EHQ-0283-0470 8EHQ-0283-0471 S
8EHQ-0483-0476 S 8EHQ-0583-0477 S 8EHQ-0683-0481
8EHQ-0683-0482 8EHQ-0783-0486 8EHQ-0883-0489
8EHQ-0883-0490 8EHQ-1083-0495 8EHQ-1083-0496
8EHQ-1283-0500 S 8EHQ-1283-0503 8EHQ-0384-0506 S
8EHQ-1083-0509 8EHQ-0484-0510 8EHQ-0484-0511
8EHQ-0484-0512 8EHQ-0584-0515 S 8EHQ-0584-0516 S
8EHQ-0584-0518 S 8EHQ-0584-0519 8EHQ-0784-0522
8EHQ-0984-0530 8EHQ-1084-0532 8EHQ-1084-0533 S

APPENDIX D: STATUS REPORTS BY INFORMATION TYPE (CONT.)

MUTAGENICITY (IN VITRO) (CONT.)			
SUBMISSION #:	8EHQ-1184-0537	8EHQ-1284-0539	8EHQ-1284-0541 S
MUTAGENICITY (IN VIVO)			
SUBMISSION #:	8EHQ-0483-0476 S	8EHQ-1083-0499	
NEUROTOXICITY (ANIMAL)			
SUBMISSION #:	8EHQ-0583-0478 S	8EHQ-1083-0494 *	8EHQ-1283-0501
	8EHQ-0684-0520	8EHQ-1084-0532	
ONCOGENICITY (ANIMAL)			
SUBMISSION #:	8EHQ-0283-0469 S	8EHQ-0283-0472 S	8EHQ-0383-0474
	8EHQ-0683-0480	8EHQ-0683-0483 S	8EHQ-0783-0486
	8EHQ-0783-0488	8EHQ-1083-0497	8EHQ-1283-0503
	8EHQ-0384-0507	8EHQ-1083-0509	8EHQ-0584-0514
	8EHQ-0584-0517	8EHQ-0884-0525	8EHQ-0884-0526
	8EHQ-0984-0530	8EHQ-1284-0538	
ONCOGENICITY (HUMAN)			
SUBMISSION #:	8EHQ-0383-0473	8EHQ-0884-0523	
PRODUCT COMPOSITION/CHEMICAL IDENTITY			
SUBMISSION #:	8EHQ-0283-0469 S	8EHQ-0283-0471 S	8EHQ-0583-0477 S
	8EHQ-0583-0479 S	8EHQ-0683-0480	8EHQ-0683-0483 S
	8EHQ-0683-0484 S	8EHQ-0783-0485 S *	8EHQ-0783-0487 S *
	8EHQ-0983-0491 S	8EHQ-0983-0493 S *	8EHQ-1283-0500 S

APPENDIX D: STATUS REPORTS BY INFORMATION TYPE (CONT.)

PRODUCT COMPOSITION/CHEMICAL IDENTITY (CONT.)

SUBMISSION #:	8EHQ-1283-0501	8EHQ-1283-0502 P *	8EHQ-1283-0503
	8EHQ-0384-0508 P *	8EHQ-0484-0510	8EHQ-0484-0511
	8EHQ-0484-0513	8EHQ-0584-0515 S	8EHQ-0584-0516 S
	8EHQ-0584-0517	8EHQ-0584-0519	8EHQ-0784-0521 S
	8EHQ-0884-0526	8EHQ-1284-0540 S *	

PRODUCTION/USE/PROCESS

SUBMISSION #:	8EHQ-0583-0477 S	8EHQ-0583-0479 S	8EHQ-0683-0480
	8EHQ-0683-0481	8EHQ-0683-0483 S	8EHQ-0783-0485 S *
	8EHQ-0783-0487 S *	8EHQ-0883-0490	8EHQ-0983-0492 S
	8EHQ-0983-0493 S *	8EHQ-1083-0494 *	8EHQ-1083-0495
	8EHQ-1083-0496	8EHQ-1083-0497	8EHQ-1083-0498
	8EHQ-1283-0500 S	8EHQ-1283-0501	8EHQ-1283-0502 P *
	8EHQ-1283-0503	8EHQ-0184-0504	8EHQ-0284-0505
	8EHQ-0384-0506 S	8EHQ-1083-0509	8EHQ-0484-0510
	8EHQ-0484-0513	8EHQ-0584-0514	8EHQ-0584-0515 S
	8EHQ-0584-0516 S	8EHQ-0584-0517	8EHQ-0584-0519
	8EHQ-0684-0520	8EHQ-0784-0521 S	8EHQ-0784-0522
	8EHQ-0884-0523	8EHQ-0884-0524	8EHQ-0884-0526
	8EHQ-0884-0528	8EHQ-0984-0529	8EHQ-0984-0531 S *
	8EHQ-1084-0532	8EHQ-1084-0533 S	8EHQ-1084-0534
	8EHQ-1084-0535		

APPENDIX D: STATUS REPORTS BY INFORMATION TYPE (CONT.)

REPORTING RATIONALE

SUBMISSION #:	8EHQ-0783-0485 S *	8EHQ-1083-0494 *	8EHQ-0384-0508 P *

REPRODUCTIVE TOXICITY/TERATO. (ANIMAL)

SUBMISSION #:	8EHQ-0483-0475	8EHQ-0783-0485 S *	8EHQ-1083-0499
	8EHQ-0284-0505	8EHQ-0884-0527	8EHQ-0884-0528
	8EHQ-1084-0532	8EHQ-1084-0534	

SUBACUTE TOXICITY (ANIMAL)

SUBMISSION #:	8EHQ-0483-0476 S	8EHQ-0583-0478 S	8EHQ-0683-0483 S
	8EHQ-0683-0484 S	8EHQ-0783-0485 S *	8EHQ-1083-0495
	8EHQ-1083-0498	8EHQ-0284-0505	8EHQ-0684-0520
	8EHQ-1084-0532	8EHQ-1084-0534	

SUBCHRONIC TOXICITY (ANIMAL)

SUBMISSION #:	8EHQ-0683-0483 S	8EHQ-1083-0494 *	8EHQ-0184-0504
	8EHQ-0384-0507	8EHQ-0884-0524	8EHQ-0984-0529

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* Based on a preliminary evaluation, EPA believes that the submitted information did not warrant reporting pursuant to Section 8(e) of TSCA. In most cases, the submitter was requested to provide the basis for the company's contention that the information offered reasonable support for the conclusion that the subject chemical(s) posed a substantial risk of injury to health or the environment as defined in the Agency's March 16, 1978 Section 8(e) policy statement (see Appendix A of this volume).

APPENDIX E: STATUS REPORTS BY SUBMISSION NUMBER

8EHQ-0183-0468 SUBMITTER: PHILLIPS PETROLEUM COMPANY

CAS NUMBER: NONE CHEMICAL NAME: CARBON BLACK FEEDSTOCK

CAS NUMBER: 64741-59-9 CHEMICAL NAME: DISTILLATES (PETROLEUM), LIGHT CATALYTIC CRACKED

CAS NUMBER: 64741-60-2 CHEMICAL NAME: DISTILLATES (PETROLEUM), INTERMEDIATE CATALYTIC CRACKED

CAS NUMBER: 64741-61-3 CHEMICAL NAME: DISTILLATES (PETROLEUM), HEAVY CATALYTIC CRACKED

8EHQ-0283-0469 S SUBMITTER: CONFIDENTIAL

CAS NUMBER: NONE CHEMICAL NAME: CUTTING FLUID

CAS NUMBER: NONE CHEMICAL NAME: NITROSAMINES

CAS NUMBER: 1116-54-7 CHEMICAL NAME: ETHANOL, 2,2'-(NITROSOIMINO)BIS-

CAS NUMBER: 1116-54-7 CHEMICAL NAME: N-NITROSODIETHANOLAMINE

8EHQ-0283-0470 SUBMITTER: ANGUS CHEMICAL COMPANY

CAS NUMBER: 51200-87-4 CHEMICAL NAME: OXAZOLIDINE, 4,4-DIMETHYL-

8EHQ-0283-0471 S SUBMITTER: FERRO CORPORATION

CAS NUMBER: NONE CHEMICAL NAME: CUTTING FLUID

CAS NUMBER: NONE CHEMICAL NAME: JP-8

CAS NUMBER: NONE CHEMICAL NAME: KLARUS 1717

CAS NUMBER: 8008-20-6 CHEMICAL NAME: KEROSINE

CAS NUMBER: 70776-26-0 CHEMICAL NAME: DISULFIDE, BIS(2-CHLOROOCTYL)

APPENDIX E: STATUS REPORTS BY SUBMISSION NUMBER (CONT.)

8EHQ-0283-0472 S SUBMITTER: CONFIDENTIAL
CAS NUMBER: 8008-20-6 CHEMICAL NAME: KEROSINE
CAS NUMBER: 64741-68-0 CHEMICAL NAME: NAPHTHA (PETROLEUM), HEAVY CATALYTIC REFORMED
CAS NUMBER: 68477-31-6 CHEMICAL NAME: DISTILLATES (PETROLEUM), CATALYTIC REFORMER FRACTIONATOR RESIDUE, LOW-BOILING

8EHQ-0383-0473 SUBMITTER: W. R. GRACE & CO.
CAS NUMBER: 1318-00-9 CHEMICAL NAME: VERMICULITE
CAS NUMBER: 14567-73-8 CHEMICAL NAME: TREMOLITE
CAS NUMBER: 77536-68-6 CHEMICAL NAME: TREMOLITE ASBESTOS

8EHQ-0383-0474 SUBMITTER: CELANESE CORPORATION
CAS NUMBER: 50-00-0 CHEMICAL NAME: FORMALDEHYDE
CAS NUMBER: 75-07-0 CHEMICAL NAME: ACETALDEHYDE

8EHQ-0483-0475 SUBMITTER: EASTMAN KODAK COMPANY
CAS NUMBER: 111-76-2 CHEMICAL NAME: ETHANOL, 2-BUTOXY-

8EHQ-0483-0476 S SUBMITTER: CONFIDENTIAL
CAS NUMBER: 382-10-5 CHEMICAL NAME: 1-PROPENE, 3,3,3-TRIFLUORO-2-(TRIFLUOROMETHYL)-

8EHQ-0583-0477 S SUBMITTER: CONFIDENTIAL
CAS NUMBER: CONFIDENT CHEMICAL NAME: AROMATICS, SUBSTITUTED

8EHQ-0583-0478 S SUBMITTER: SHELL OIL COMPANY
CAS NUMBER: 51365-70-9 CHEMICAL NAME: EPON CURING AGENT D
CAS NUMBER: 51365-70-9 CHEMICAL NAME: HEXANOIC ACID, 2-ETHYL-, COMPD. WITH 2,4,6-TRIS[(DIMETHYLAMINO)METHYL]PHENOL

APPENDIX E: STATUS REPORTS BY SUBMISSION NUMBER (CONT.)

8EHQ-0583-0479 S SUBMITTER: CONFIDENTIAL

CAS NUMBER: NONE CHEMICAL NAME: CONFIDENTIAL
CAS NUMBER: 9003-07-0 CHEMICAL NAME: POLYPROPYLENE
CAS NUMBER: 9003-07-0 CHEMICAL NAME: 1-PROPENE, HOMOPOLYMER
CAS NUMBER: 61791-44-4 CHEMICAL NAME: ETHANOL, 2,2'-IMINOBIS-, N-TALLOW ALKYL DERIVS.

8EHQ-0683-0480 SUBMITTER: EXXON COMPANY, U.S.A.

CAS NUMBER: 64742-30-9 CHEMICAL NAME: DISTILLATES (PETROLEUM), CHEMICALLY NEUTRALIZED MIDDLE
CAS NUMBER: 64742-30-9 CHEMICAL NAME: MENTOR 28
CAS NUMBER: 64742-30-9 CHEMICAL NAME: SOMENTOR 43

8EHQ-0683-0481 SUBMITTER: PHILLIPS PETROLEUM COMPANY

CAS NUMBER: 540-63-6 CHEMICAL NAME: 1,2-ETHANEDITHIOL

8EHQ-0683-0482 SUBMITTER: INTERNATIONAL COAL REFINING COMPANY

CAS NUMBER: NONE CHEMICAL NAME: COAL, SOLVENT-REFINING (SRC) PROCESS/PRODUCTS
CAS NUMBER: NONE CHEMICAL NAME: SRC PROCESS/PRODUCTS
CAS NUMBER: UNKNOWN CHEMICAL NAME: DISTILLATES (COAL), SOLVENT-REFINING (SRC), MIDDLE, TWO STAGE LIQUEFACTION (TSL)
CAS NUMBER: UNKNOWN CHEMICAL NAME: FUEL, TSL SOLID
CAS NUMBER: UNKNOWN CHEMICAL NAME: RESIDUES (COAL), SOLVENT-REFINING (SRC), VACUUM-DISTN., TWO STAGE LIQUEFACTION (TSL)
CAS NUMBER: 68131-74-8 CHEMICAL NAME: ASHES (RESIDUES)
CAS NUMBER: 68409-94-9 CHEMICAL NAME: FUEL, SRC SOLID

APPENDIX E: STATUS REPORTS BY SUBMISSION NUMBER (CONT.)

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8EHQ-0683-0482      (CONT.)  SUBMITTER: INTERNATIONAL COAL REFINING COMPANY
         CAS NUMBER:  68409-94-9       CHEMICAL NAME: RESIDUES (COAL), SOLVENT-REFINING (SRC), VACUUM-DISTN.
         CAS NUMBER:  68476-79-9       CHEMICAL NAME: NAPHTHA (COAL), SOLVENT-REFINING
         CAS NUMBER:  68911-57-9       CHEMICAL NAME: DISTILLATES (COAL), SOLVENT-REFINING (SRC), MIDDLE

8EHQ-0683-0483 S             SUBMITTER: CONFIDENTIAL
         CAS NUMBER:  CONFIDENT        CHEMICAL NAME: CONFIDENTIAL
         CAS NUMBER:  1429-50-1        CHEMICAL NAME: PHOSPHONIC ACID, [1,2-ETHANEDIYLBIS[NITRILOBIS(METHYLENE)]]T
                                                      ETRAKIS-

8EHQ-0683-0484 S             SUBMITTER: ROHM AND HAAS COMPANY
         CAS NUMBER:  CONFIDENT        CHEMICAL NAME: ACRYLIC POLYMER

8EHQ-0783-0485 S   *         SUBMITTER: CIBA-GEIGY CORPORATION
         CAS NUMBER:  5915-41-3        CHEMICAL NAME: TERBUTHYLAZINE
         CAS NUMBER:  5915-41-3        CHEMICAL NAME: 1,3,5-TRIAZINE-2,4-DIAMINE, 6-CHLORO-N-(1,1-DIMETHYLETHYL)-N
                                                      '-ETHYL-

8EHQ-0783-0486               SUBMITTER: ALLIED CORPORATION
         CAS NUMBER:  10039-54-0       CHEMICAL NAME: HYDROXYLAMINE, SULFATE (2:1) (SALT)

8EHQ-0783-0487 S   *         SUBMITTER: AMERICAN CYANAMID COMPANY
         CAS NUMBER:  UNKNOWN          CHEMICAL NAME: NICOTINIC ACID DERIVATIVE
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APPENDIX E: STATUS REPORTS BY SUBMISSION NUMBER (CONT.)

8EHQ-0783-0488 SUBMITTER: DOW CHEMICAL COMPANY
CAS NUMBER: 79-06-1 CHEMICAL NAME: ACRYLAMIDE
CAS NUMBER: 79-06-1 CHEMICAL NAME: 2-PROPENAMIDE

8EHQ-0883-0489 SUBMITTER: LONZA INC.
CAS NUMBER: 68479-98-1 CHEMICAL NAME: BENZENEDIAMINE, AR,AR-DIETHYL-AR-METHYL-

8EHQ-0883-0490 SUBMITTER: CIBA-GEIGY CORPORATION
CAS NUMBER: NONE CHEMICAL NAME: EPOXY RESINS
CAS NUMBER: 2451-62-9 CHEMICAL NAME: ARALDITE PT-810
CAS NUMBER: 2451-62-9 CHEMICAL NAME: 1,3,5-TRIAZINE-2,4,6(1H,3H,5H)-TRIONE, 1,3,5-TRIS(OXIRANYLMETHYL)-

8EHQ-0983-0491 S SUBMITTER: CHLORINATED PARAFFIN PRODUCERS TESTING CONSORTIUM
CAS NUMBER: 63449-39-8 CHEMICAL NAME: CHLORINATED PARAFFINS
CAS NUMBER: 63449-39-8 CHEMICAL NAME: PARAFFIN WAXES AND HYDROCARBON WAXES, CHLORINATED

8EHQ-0983-0492 S SUBMITTER: CONFIDENTIAL
CAS NUMBER: CONFIDENT CHEMICAL NAME: CARBAMATE, ALIPHATIC

8EHQ-0983-0493 S * SUBMITTER: CONFIDENTIAL
CAS NUMBER: CONFIDENT CHEMICAL NAME: OXIDES, METALLIC (MIXTURE)

APPENDIX E: STATUS REPORTS BY SUBMISSION NUMBER (CONT.)

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8EHQ-1083-0494      *           SUBMITTER: PPG INDUSTRIES, INC.
          CAS NUMBER:  20762-60-1        CHEMICAL NAME: POTASSIUM AZIDE (K(N3))
          CAS NUMBER:  26628-22-8        CHEMICAL NAME: SODIUM AZIDE (NA(N3))

8EHQ-1083-0495                  SUBMITTER: EASTMAN KODAK COMPANY
          CAS NUMBER:  1134-36-7         CHEMICAL NAME: [1,1'-BIPHENYL]-4-OL, 3-AMINO-

8EHQ-1083-0496                  SUBMITTER: EASTMAN KODAK COMPANY
          CAS NUMBER:  89-62-3           CHEMICAL NAME: BENZENAMINE, 4-METHYL-2-NITRO-

8EHQ-1083-0497                  SUBMITTER: E. I. DUPONT DE NEMOURS & COMPANY, INC.
          CAS NUMBER:  13463-67-7        CHEMICAL NAME: TITANIUM OXIDE (TIO2)

8EHQ-1083-0498                  SUBMITTER: GULF OIL CHEMICALS COMPANY
          CAS NUMBER:  64742-90-1        CHEMICAL NAME: RESIDUES (PETROLEUM), STEAM-CRACKED

8EHQ-1083-0499                  SUBMITTER: VULCAN CHEMICALS
          CAS NUMBER:  74-87-3           CHEMICAL NAME: METHANE, CHLORO-

8EHQ-1283-0500 S                SUBMITTER: CONFIDENTIAL
          CAS NUMBER:  CONFIDENT         CHEMICAL NAME: BENZENAMINE, SUBSTITUTED POLYGLYCIDYL

8EHQ-1283-0501                  SUBMITTER: CHEVRON CHEMICAL COMPANY
          CAS NUMBER:  79419-43-5        CHEMICAL NAME: 2-CYCLOHEXEN-1-ONE, 2-(2-OXOBUTYL)-5-(2-ETHYLTHIO)-PROPYL-3-
                                                        HYDROXY-
          CAS NUMBER:  79419-43-5        CHEMICAL NAME: ORTHO 36015
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APPENDIX E: STATUS REPORTS BY SUBMISSION NUMBER (CONT.)

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8EHQ-1283-0502 P   *       SUBMITTER: GENERAL MOTORS CORPORATION
          CAS NUMBER:  NONE           CHEMICAL NAME: HYPALON MOLDING COMPOUND (THERMAL-DECOMPOSITION PRODUCTS)
          CAS NUMBER:  NONE           CHEMICAL NAME: MISC. CHEMICALS

8EHQ-1283-0503             SUBMITTER: DOW CHEMICAL COMPANY
          CAS NUMBER:  3033-77-0      CHEMICAL NAME: G-MAC
          CAS NUMBER:  3033-77-0      CHEMICAL NAME: OXIRANEMETHANAMINIUM, N,N,N-TRIMETHYL-, CHLORIDE
          CAS NUMBER:  3327-22-8      CHEMICAL NAME: 1-PROPANAMINIUM, 3-CHLORO-2-HYDROXY-N,N,N-TRIMETHYL-, CHLORI
                                                     DE

8EHQ-0184-0504             SUBMITTER: RIO BLANCO OIL SHALE COMPANY
          CAS NUMBER:  UNKNOWN        CHEMICAL NAME: OIL (SHALE), LURGI LIGHT/MIDDLE
          CAS NUMBER:  68308-34-9     CHEMICAL NAME: SHALE OILS

8EHQ-0284-0505             SUBMITTER: STANDARD OIL COMPANY (INDIANA)
          CAS NUMBER:  64741-88-4     CHEMICAL NAME: DISTILLATES (PETROLEUM), SOLVENT-REFINED HEAVY PARAFFINIC
          CAS NUMBER:  64742-65-0     CHEMICAL NAME: DISTILLATES (PETROLEUM), SOLVENT-DEWAXED HEAVY PARAFFINIC

8EHQ-0384-0506 S           SUBMITTER: CONFIDENTIAL
          CAS NUMBER:  959-52-4       CHEMICAL NAME: 1,3,5-TRIAZINE, HEXAHYDRO-1,3,5-TRIS(1-OXO-2-PROPENYL)-

8EHQ-0384-0507             SUBMITTER: GULF OIL PRODUCTS COMPANY
          CAS NUMBER:  64741-53-3     CHEMICAL NAME: DISTILLATES (PETROLEUM), HEAVY NAPHTHENIC
          CAS NUMBER:  64741-53-3     CHEMICAL NAME: GULF 100 TEXAS DISTILLATE
          CAS NUMBER:  64742-11-6     CHEMICAL NAME: EXTRACTS (PETROLEUM), HEAVY NAPHTHENIC DISTILLATE SOLVENT
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                         APPENDIX E:  STATUS REPORTS BY SUBMISSION NUMBER (CONT.)
8EHQ-0384-0507       (CONT.)  SUBMITTER: GULF OIL PRODUCTS COMPANY
        CAS NUMBER:  64742-11-6      CHEMICAL NAME: GULF N.E. 61 (PROCESS 65)
        CAS NUMBER:  64742-52-5      CHEMICAL NAME: DISTILLATES (PETROLEUM), HYDROTREATED HEAVY NAPHTHENIC
        CAS NUMBER:  64742-52-5      CHEMICAL NAME: GULF 100 TEXAS OIL
8EHQ-0384-0508 P   *          SUBMITTER: RACON INC.
        CAS NUMBER:  NONE            CHEMICAL NAME: MISC. CHEMICALS
        CAS NUMBER:  7647-01-0       CHEMICAL NAME: HYDROCHLORIC ACID
        CAS NUMBER:  7647-18-9       CHEMICAL NAME: ANTIMONY CHLORIDE (SBCL5)
        CAS NUMBER:  7664-39-3       CHEMICAL NAME: HYDROFLUORIC ACID
8EHQ-1083-0509                SUBMITTER: UNION CARBIDE CORPORATION
        CAS NUMBER:  64-67-5         CHEMICAL NAME: SULFURIC ACID, DIETHYL ESTER
8EHQ-0484-0510                SUBMITTER: IBM CORPORATION
        CAS NUMBER:  1143-72-2       CHEMICAL NAME: METHANONE, PHENYL(2,3,4-TRIHYDROXYPHENYL)-
8EHQ-0484-0511                SUBMITTER: GULF OIL PRODUCTS COMPANY
        CAS NUMBER:  NONE            CHEMICAL NAME: 1,3-BUTADIENE FEEDSTOCK
        CAS NUMBER:  75-28-5         CHEMICAL NAME: PROPANE, 2-METHYL-
        CAS NUMBER:  106-97-8        CHEMICAL NAME: BUTANE
        CAS NUMBER:  106-98-9        CHEMICAL NAME: 1-BUTENE
        CAS NUMBER:  106-99-0        CHEMICAL NAME: 1,3-BUTADIENE
        CAS NUMBER:  115-11-7        CHEMICAL NAME: 1-PROPENE, 2-METHYL-
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APPENDIX E: STATUS REPORTS BY SUBMISSION NUMBER (CONT.)

8EHQ-0484-0511 (CONT.) SUBMITTER: GULF OIL PRODUCTS COMPANY
CAS NUMBER: 25167-67-3 CHEMICAL NAME: BUTENE

8EHQ-0484-0512 SUBMITTER: GULF OIL PRODUCTS COMPANY
CAS NUMBER: NONE CHEMICAL NAME: GREASE, GULFCROWN E.P. NO. 2
CAS NUMBER: NONE CHEMICAL NAME: GULFCROWN GREASE E.P. NO. 2
CAS NUMBER: NONE CHEMICAL NAME: ZINC DIALKYL DITHIOPHOSPHATES (ZDDP)
CAS NUMBER: UNKNOWN CHEMICAL NAME: ZINC DIAMYL DITHIOCARBAMATES
CAS NUMBER: 63449-39-8 CHEMICAL NAME: CHLORINATED PARAFFINS
CAS NUMBER: 63449-39-8 CHEMICAL NAME: PARAFFIN WAXES AND HYDROCARBON WAXES, CHLORINATED
CAS NUMBER: 64742-54-7 CHEMICAL NAME: DISTILLATES (PETROLEUM), HYDROTREATED HEAVY PARAFFINIC
CAS NUMBER: 64742-57-0 CHEMICAL NAME: RESIDUAL OILS (PETROLEUM), HYDROTREATED

8EHQ-0484-0513 SUBMITTER: MALLINCKRODT, INC.
CAS NUMBER: 51-78-5 CHEMICAL NAME: PHENOL, 4-AMINO-, HYDROCHLORIDE
CAS NUMBER: 62-53-3 CHEMICAL NAME: BENZENAMINE
CAS NUMBER: 67-56-1 CHEMICAL NAME: METHANOL
CAS NUMBER: 98-95-3 CHEMICAL NAME: BENZENE, NITRO-
CAS NUMBER: 100-65-2 CHEMICAL NAME: BENZENAMINE, N-HYDROXY-
CAS NUMBER: 103-33-3 CHEMICAL NAME: DIAZENE, DIPHENYL-
CAS NUMBER: 123-30-8 CHEMICAL NAME: PHENOL, 4-AMINO-
CAS NUMBER: 495-48-7 CHEMICAL NAME: DIAZENE, DIPHENYL-, 1-OXIDE
CAS NUMBER: 7803-49-8 CHEMICAL NAME: HYDROXYLAMINE

APPENDIX E: STATUS REPORTS BY SUBMISSION NUMBER (CONT.)

8EHQ-0584-0514 SUBMITTER: CELANESE CORPORATION
- CAS NUMBER: 109-52-4 CHEMICAL NAME: PENTANOIC ACID
- CAS NUMBER: 111-14-8 CHEMICAL NAME: HEPTANOIC ACID
- CAS NUMBER: 112-05-0 CHEMICAL NAME: NONANOIC ACID

8EHQ-0584-0515 S SUBMITTER: CONFIDENTIAL
- CAS NUMBER: NONE CHEMICAL NAME: EPOXY RESINS

8EHQ-0584-0516 S SUBMITTER: CONFIDENTIAL
- CAS NUMBER: NONE CHEMICAL NAME: EPOXY RESINS
- CAS NUMBER: 9003-11-6 CHEMICAL NAME: OXIRANE, METHYL-, POLYMER WITH OXIRANE

8EHQ-0584-0517 SUBMITTER: EXXON COMPANY, U.S.A.
- CAS NUMBER: CONFIDENT CHEMICAL NAME: OXIDIZED WAX ACIDS, CALCIUM SOAP
- CAS NUMBER: CONFIDENT CHEMICAL NAME: PETROLEUM SULFONATE, CALCIUM
- CAS NUMBER: NONE CHEMICAL NAME: RUST-BAN 392
- CAS NUMBER: 111-76-2 CHEMICAL NAME: ETHANOL, 2-BUTOXY-
- CAS NUMBER: 8052-41-3 CHEMICAL NAME: SOLVENT, STODDARD
- CAS NUMBER: 8052-41-3 CHEMICAL NAME: STODDARD SOLVENT
- CAS NUMBER: 64741-62-4 CHEMICAL NAME: CLARIFIED OILS (PETROLEUM), CATALYTIC CRACKED

8EHQ-0584-0518 S SUBMITTER: CONFIDENTIAL
- CAS NUMBER: NONE CHEMICAL NAME: EPON 815
- CAS NUMBER: NONE CHEMICAL NAME: EPOXY RESINS

APPENDIX E: STATUS REPORTS BY SUBMISSION NUMBER (CONT.)

8EHQ-0584-0518 S (CONT.) SUBMITTER: CONFIDENTIAL

CAS NUMBER: 106-89-8 CHEMICAL NAME: EPICHLOROHYDRIN
CAS NUMBER: 106-89-8 CHEMICAL NAME: OXIRANE, (CHLOROMETHYL)-
CAS NUMBER: 2426-08-6 CHEMICAL NAME: BUTYL GLYCIDYL ETHER
CAS NUMBER: 2426-08-6 CHEMICAL NAME: OXIRANE, (BUTOXYMETHYL)-
CAS NUMBER: 25068-38-6 CHEMICAL NAME: PHENOL, 4,4'-(1-METHYLETHYLIDENE)BIS-, POLYMER WITH (CHLOROMETHYL)OXIRANE

8EHQ-0584-0519 SUBMITTER: 3M COMPANY

CAS NUMBER: UNKNOWN CHEMICAL NAME: 2-THIAZOLIUM, 2,2'-[(2-CARBOXY-P-PHENYLENE)BIS(IMINOVINYLENE)]BIS(3-ETHYL)DIIODIDE, TRIETHYLAMINE SALT
CAS NUMBER: 20328-87-4 CHEMICAL NAME: PINA SENSITIZER KF 501
CAS NUMBER: 20328-87-4 CHEMICAL NAME: 2-THIAZOLIUM, 2,2'-[(2-CARBOXY-P-PHENYLENE)BIS(IMINOVINYLENE)]BIS(3-ETHYL)DIIODIDE

8EHQ-0684-0520 SUBMITTER: CIBA-GEIGY CORPORATION

CAS NUMBER: 71868-10-5 CHEMICAL NAME: IRGACURE 907
CAS NUMBER: 71868-10-5 CHEMICAL NAME: 1-PROPANONE, 2-METHYL-1-[(4-METHYLTHIO)PHENYL]-2-(4-MORPHOLINYL)-

8EHQ-0784-0521 S SUBMITTER: EMHART CORPORATION

CAS NUMBER: 1336-36-3 CHEMICAL NAME: 1,1'-BIPHENYL, CHLORO DERIVS.
CAS NUMBER: 1336-36-3 CHEMICAL NAME: POLYCHLORINATED BIPHENYLS (PCB)

APPENDIX E: STATUS REPORTS BY SUBMISSION NUMBER (CONT.)

8EHQ-0784-0522 SUBMITTER: WITCO CHEMICAL CORPORATION
CAS NUMBER: 2386-87-0 CHEMICAL NAME: 7-OXABICYCLO[4.1.0]HEPTANE-3-CARBOXYLIC ACID, 7-OXABICYCLO[4.1.0]HEPT-3-YLMETHYL ESTER
CAS NUMBER: 26544-23-0 CHEMICAL NAME: PHOSPHOROUS ACID, ISODECYL DIPHENYL ESTER

8EHQ-0884-0523 SUBMITTER: VELSICOL CHEMICAL CORPORATION
CAS NUMBER: 98-07-7 CHEMICAL NAME: BENZENE, (TRICHLOROMETHYL)-
CAS NUMBER: 98-88-4 CHEMICAL NAME: BENZOYL CHLORIDE
CAS NUMBER: 100-44-7 CHEMICAL NAME: BENZENE, (CHLOROMETHYL)-

8EHQ-0884-0524 SUBMITTER: UNION CARBIDE CORPORATION
CAS NUMBER: 2530-85-0 CHEMICAL NAME: 2-PROPENOIC ACID, 2-METHYL-, 3-(TRIMETHOXYSILYL)PROPYL ESTER
CAS NUMBER: 2530-85-0 CHEMICAL NAME: SILANE A-174

8EHQ-0884-0525 SUBMITTER: HALOGENATED SOLVENTS INDUSTRY ALLIANCE
CAS NUMBER: 75-09-2 CHEMICAL NAME: METHANE, DICHLORO-
CAS NUMBER: 75-09-2 CHEMICAL NAME: METHYLENE CHLORIDE

8EHQ-0884-0526 SUBMITTER: UNION CARBIDE CORPORATION
CAS NUMBER: UNKNOWN CHEMICAL NAME: OIL, UNSATURATED ALIPHATIC (C16-C32)

8EHQ-0884-0527 SUBMITTER: CHLORINATED PARAFFIN PRODUCERS TESTING CONSORTIUM
CAS NUMBER: 63449-39-8 CHEMICAL NAME: CHLORINATED PARAFFINS
CAS NUMBER: 63449-39-8 CHEMICAL NAME: PARAFFIN WAXES AND HYDROCARBON WAXES, CHLORINATED

APPENDIX E: STATUS REPORTS BY SUBMISSION NUMBER (CONT.)

8EHQ-0884-0528 SUBMITTER: DOW CHEMICAL COMPANY
CAS NUMBER: 122-99-6 CHEMICAL NAME: ETHANOL, 2-PHENOXY-

8EHQ-0984-0529 SUBMITTER: EASTMAN KODAK COMPANY
CAS NUMBER: 92-43-3 CHEMICAL NAME: PHENIDONE
CAS NUMBER: 92-43-3 CHEMICAL NAME: 3-PYRAZOLIDINONE, 1-PHENYL-

8EHQ-0984-0530 SUBMITTER: E. I. DUPONT DE NEMOURS & COMPANY, INC.
CAS NUMBER: 7550-45-0 CHEMICAL NAME: TITANIUM CHLORIDE (TICL4), (T-4)-

8EHQ-0984-0531 S * SUBMITTER: CONFIDENTIAL
CAS NUMBER: 68442-97-7 CHEMICAL NAME: 1H-IMIDAZOLE-1-ETHANAMINE, 4,5-DIHYDRO-, 2-NORTALL-OIL ALKYL DERIVS.

8EHQ-1084-0532 SUBMITTER: ALLIED CORPORATION
CAS NUMBER: 76379-66-3 CHEMICAL NAME: 5,7,11-DODECATRIYN-1-OL

8EHQ-1084-0533 S SUBMITTER: CONFIDENTIAL
CAS NUMBER: 69045-78-9 CHEMICAL NAME: PYRIDINE, 2-CHLORO-5-TRICHLOROMETHYL-

8EHQ-1084-0534 SUBMITTER: TENNESSEE EASTMAN COMPANY
CAS NUMBER: 111-07-9 CHEMICAL NAME: HEXADECANOIC ACID, 2-METHOXYETHYL ESTER

8EHQ-1084-0535 SUBMITTER: 3M COMPANY
CAS NUMBER: NONE CHEMICAL NAME: PERFLUOROALKYL COMPOUNDS
CAS NUMBER: 71-55-6 CHEMICAL NAME: ETHANE, 1,1,1-TRICHLORO-

APPENDIX E: STATUS REPORTS BY SUBMISSION NUMBER (CONT.)

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8EHQ-1084-0535       (CONT.)  SUBMITTER: 3M COMPANY

         CAS NUMBER:  76-13-1        CHEMICAL NAME: ETHANE, 1,1,2-TRICHLORO-1,2,2-TRIFLUORO-

         CAS NUMBER:  76-13-1        CHEMICAL NAME: FREON 113

         CAS NUMBER:  108-10-1       CHEMICAL NAME: 2-PENTANONE, 4-METHYL-

         CAS NUMBER:  10212-58-5     CHEMICAL NAME: 1-AZIRIDINECARBOXAMIDE, 2-METHYL-N-OCTADECYL-

         CAS NUMBER:  68298-78-2     CHEMICAL NAME: PERFLUOROALKYL RESIN

         CAS NUMBER:  68298-78-2     CHEMICAL NAME: 2-PROPENOIC ACID, 2-METHYL-, 2-[[[[5-[[[2-[ETHYL[(HEPTADECAF
                                                    LUOROOCTYL)SULFONYL]AMINO]ETHOXY]CARBONYL]AMINO]-2-METHYLPHE
                                                    NYL]AMINO]CARBONYL]OXY]PROPYL ESTER, TELOMER WITH BUTYL 2-PR
                                                    OPENOATE, 2-[[[[5-[[[2-[ETHYL[(NONAFLUOROBUTYL)SULFONYL]AMIN
                                                    O]ETHOXY]CARBONYL]AMINO]-2-METHYLPHENYL]AMINO]CARBONYL]OXY]P

         CAS NUMBER:  68555-92-0     CHEMICAL NAME: PERFLUOROALKYL RESIN

         CAS NUMBER:  68555-92-0     CHEMICAL NAME: 2-PROPENOIC ACID, 2-METHYL-, 2-[[(HEPTADECAFLUOROOCTYL)SULFO
                                                    NYL]METHYLAMINO]ETHYL ESTER, POLYMER WITH 2-[METHYL[(NONAFLU
                                                    OROBUTYL)SULFONYL]AMINO]ETHYL 2-METHYL-2-PROPENOATE, 2-[METH
                                                    YL[(PENTADECAFLUOROHEPTYL)SULFONYL]AMINO]ETHYL 2-METHYL-2-PR
                                                    OPENOATE, 2-[METHYL[(TRIDECAFLUOROHEXYL)SULFONYL]AMINO]ETHYL

8EHQ-1184-0536                SUBMITTER: GULF OIL PRODUCTS COMPANY

         CAS NUMBER:  98-82-8        CHEMICAL NAME: BENZENE, (1-METHYLETHYL)-

         CAS NUMBER:  98-82-8        CHEMICAL NAME: CUMENE

8EHQ-1184-0537                SUBMITTER: GULF OIL PRODUCTS COMPANY

         CAS NUMBER:  UNKNOWN        CHEMICAL NAME: FUEL OIL, LIGHT PYROLYSIS

         CAS NUMBER:  69013-21-4     CHEMICAL NAME: FUEL OILS, PYROLYSIS
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APPENDIX E: STATUS REPORTS BY SUBMISSION NUMBER (CONT.)

8EHQ-1284-0538 SUBMITTER: AIR PRODUCTS AND CHEMICALS, INC.

CAS NUMBER: NONE CHEMICAL NAME: COAL, SOLVENT-REFINING (SRC) PROCESS/PRODUCTS
CAS NUMBER: NONE CHEMICAL NAME: SRC PROCESS/PRODUCTS
CAS NUMBER: UNKNOWN CHEMICAL NAME: DUST, SRC SOLID

8EHQ-1284-0539 SUBMITTER: NOR-AM CHEMICAL COMPANY

CAS NUMBER: 87-66-1 CHEMICAL NAME: 1,2,3-BENZENETRIOL
CAS NUMBER: 87-66-1 CHEMICAL NAME: PYROGALLOL

8EHQ-1284-0540 S * SUBMITTER: CONFIDENTIAL

CAS NUMBER: 288-32-4 CHEMICAL NAME: 1H-IMIDAZOLE
CAS NUMBER: 931-36-2 CHEMICAL NAME: 1H-IMIDAZOLE, 2-ETHYL-4-METHYL-

8EHQ-1284-0541 S SUBMITTER: CONFIDENTIAL

CAS NUMBER: 480-96-6 CHEMICAL NAME: BENZOFURAZAN, 1-OXIDE

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* Based on a preliminary evaluation, EPA believes that the submitted information did not warrant reporting pursuant to Section 8(e) of TSCA. In most cases, the submitter was requested to provide the basis for the company's contention that the information offered reasonable support for the conclusion that the subject chemical(s) posed a substantial risk of injury to health or the environment as defined in the Agency's March 16, 1978 Section 8(e) policy statement (see Appendix A of this volume).